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(54) Title: GENTLE-ACTING SKIN-DISINFECTANTS AND HYDROALCOHOLIC GEL FORMULATIONS

(57) Abstract: Antimicrobial compositions having synergistic combinations of octoxyglycerin and at least one other antimicrobial agent in formulations which are more effective than prior art compositions without causing increased irritation to the skin of the average user. In certain embodiments, skin irritation may be minimized by low concentrations of antimicrobials and/or the presence of soothing compounds such as zinc. Preferred embodiments include combinations of octoxyglycerin, a quaternary compound, and at least one other antimicrobial agent. Without being bound to any particular theory, it is hypothesized that the unexpected antimicrobial effectiveness of combinations of octoxyglycerin may result from an enhancement of the permeability of microbes to antimicrobials caused by octoxyglycerin. Hydroalcoholic gel composition containing alcohol, water, hydrogel, and emollient or emulsifier, wherein the composition has a viscosity of below 2000 centipoises at between 20 and 40 °C. This skin-friendly hydroalcoholic gel composition, which can be further combined with silicone polymer, emollient solvent, thickening agent and antimicrobial agent, enhances rapid and long-term antimicrobial efficacy.

GENTLE-ACTING SKIN-DISINFECTANTS AND HYDROALCOHOLIC GEL FORMULATIONS

SPECIFICATION

1. INTRODUCTION

The present invention provides for skin-friendly antimicrobial compositions comprising synergistic combinations of octoxyglycerin and a low concentration of an antibiotic, particularly chlorhexidine. In particular embodiments, the compositions further comprise a quaternary ammonium compound that enhances killing of microbes.

The present invention further provides for skin-friendly hydroalcoholic gel formulations having antimicrobial properties and having properties of enhancing the effect of antimicrobial agents in formulation. In particular, these gel compositions comprise a low concentration of hydrogel soluble in water at ambient temperatures in combination with a low concentration of emulsifier soluble in alcohol at ambient temperature or a low concentration of emollient or mixtures thereof, such that the hydroalcoholic gel formulation has a low viscosity, preferably below 2000 centipoises at 20 to 40 °C.

2. BACKGROUND OF THE INVENTION

"Skin disinfectants" are routinely used in professional and non-professional contexts to rapidly kill microbes. A physician has a need to disinfect his or her skin both before and after examining a patient. Prior to the performance of an invasive medical procedure, the skin of the subject must be properly cleaned to avoid post-procedure infections. In non-professional contexts, a commuter, riding public transportation, may wish to disinfect her hands before handling food; a child, playing in a park, may need to clean his hands but not have the convenience of soap and water nearby. Each of these situations require, optimally, a skin disinfectant that is effective, easy to use, and non-irritating so as to permit repeated use.

A number of skin disinfectants have been developed that use alcohol as the primary antimicrobial agent. There are two general problems associated with alcohol-based disinfectants. First, the effective concentration of alcohol, generally regarded to be greater than about 60 percent weight (hereafter, all percentages should be considered weight/volume percentages, unless specified otherwise) of ethanol, or

its equivalent, is irritating to the skin, causing dryness and consequent peeling and cracking. Because chapped skin tends to be more susceptible to microbial contamination, repeated use of alcohol disinfectants can exacerbate the very problem they are intended to solve. Second, whereas alcohol can be an effective disinfectant, once it evaporates its antimicrobial activity is lost.

Alcohol-based skin disinfectants which are known in the art, some of which address the two problems mentioned above, include the following.

United States Patent No. 6,107, 261 by Taylor et al., issued August 22, 2000, and its continuations-in-part, United States Patent No. 6,204,230 by Taylor et al., issued March 20, 2001 and United States Patent No. 6,136,771 by Taylor et al., issued October 24, 2000, disclose antibacterial compositions which contain an antibacterial agent at a percent saturation of at least 50 percent. The compositions further comprise, as solubility promoters, a surfactant and a hydric solvent, which may be an alcohol.

United States Patent No. 5,776,430 by Osborne et al., issued July 7, 1998, discloses a topical antimicrobial cleaner containing about 0.65 -0.85 percent chlorhexidine and about 50-60 percent denatured alcohol, which is scrubbed onto and then rinsed off the skin.

European Patent Application 0604 848 discloses a gel comprising an antimicrobial agent, 40-90 percent by weight of an alcohol, and a polymer and thickening agent.

United States Patent No. 4,956,170 by Lee, issued September 11, 1990 relates to a high alcohol content antimicrobial gel composition which comprises various emollients and a humectant to protect the skin from the drying effects of the alcohol. In alcohol formulations, higher levels of alcohol are needed to provide instant kill against sensitive as well as resistant strains of bacteria.

Certain formulations virtually omit alcohol as a primary antimicrobial agent, such as, for example, the skin sanitizing compositions disclosed in United States Patent No. 6,187,327 by Stack, issued February 13, 2001, which comprises triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether; concentration 0.1-0.35 weight percent) in a topical lotion comprised of a surfactant phase and a wax phase, which purportedly provides antimicrobial protection for 3-4 hours after application. The composition prepared according to the claims of United States Patent No. 6,187,327 further comprises chlorhexidine digluconate.

United States Patent No. 5,965,610 by Modak et al., issued October 12, 1999, teaches skin cleaning compositions comprising antimicrobial agents and zinc salts, where zinc salts have a soothing effect on the skin. The claimed subject matter includes formulations comprising a gel formed between zinc gluconate, chlorhexidine gluconate and a solvent, to which various thickening agents, emulsifying agents and/or emollients may be added.

United States Patent No. 5,985,918 by Modak et al., issued November 16, 1999, relates to "Zinc-Based Anti-Irritant Creams".

United States Patent No. 5,705,532 by Modak et al., issued January 6, 1998, relates to "Triple Antimicrobial Compositions" comprising less than or equal to two percent of a chlorhexidine compound, less than or equal to 0.1 percent of a quaternary ammonium compound, and less than or equal to two percent parachlorometaxylenol.

Octoxyglycerin, sold under the trade name Sensiva® SC50 (Schulke & Mayr), is a glycerol alkyl ether known to be gentle to the skin. Octoxyglycerin exhibits antimicrobial activity against a variety of Gram-positive bacteria associated with perspiration odor, such as *Micrococcus luteus*, *Corynebacterium aquaticum*, *Corynebacterium flavescens*, *Corynebacterium callunae*, and *Corynebacterium nephredi*, and is used in various skin deodorant preparations at concentrations between about 0.2 and 3 percent (Sensiva® product literature, Schulke & Mayr).

For example, United States Patent No. 5,885,562 by Lowry et al., issued March 23, 1999, relates to deodorant compositions comprising an antimicrobial agent, namely polyhexamethylene biguanide (at a concentration of between 0.01 and 0.5 percent), together with a polarity modifier such as Sensiva®SC50, at levels of typically 1-15 percent. Compositions disclosed in United States Patent No. 5,885,562 may further comprise a short chain monohydric alcohol such as ethanol at a level of between 20 and 80 percent. Formulations useful as deodorants, however, would differ from those used as skin sanitizers in that skin sanitizers would optimally exhibit rapid broad spectrum activity against bacteria, fungi, and viruses, not merely gram positive odor causing bacteria.

United States Patent No. 5,516,510 by Beilfuss et al., issued May 14, 1996, discloses deodorant compositions which comprise glycerin monoalkyl ethers such as octoxyglycerin (referred to therein as 2-ethyl hexyl glycerin ether, and as

being the most preferred among these compounds). The deodorant compositions of United States Patent No. 5,516,510 may be formulated in aqueous and/or alcoholic solutions and may further comprise additional antimicrobial compounds, including triclosan, chlorhexidine salts, alexidine salts, and phenoxyethanol, among others. Specific concentration ranges for triclosan and the biguanides are not provided.

United States Patent No. 5,951,993 by Scholz et al., issued on September 14, 1999, and United States Patent No. 6,352,701 by Scholz et al., issued March 5, 2002, which is a continuation application thereof, each relate to hydroalcoholic compositions having a lower alcohol and water in a weight ratio of about 35:65 to 100:0, between at least 0.5% and 8.0% by weight thickener system of at least two emulsifiers, wherein each emulsifier is present in at least 0.05% by weight, wherein the composition free of auxiliary thickeners has a viscosity of at least 4000 centipoise at 23°C, and wherein each emulsifier is comprised of at least one hydrophilic group.

United States Patent No. 6,022,551 by Jampani et al., issued February 8, 2000, relates to an antimicrobial alcohol-containing composition containing specified antimicrobial compositions in solution with greater than 30% by volume of alcohol and a carbomer polymer thickener having a viscosity of greater than 9000 centipoise. Optional ingredients further include essential oils, tack modifiers, fragrances, emollients, pH adjusters, viscosity modifiers, transdermal enhancers, sarfactants, dyes, colors and water.

United States Patent No. 5,403,864 by Bruch et al., issued April 4, 1995, relates to alcohol-based solution containing 40-70% by weight of an alcohol or alcohol mixture, antimicrobial compounds such as triclosan and chloroxylenol (PCMX), and optionally includes emollients, surfactants, perfuming agents and chelating agents.

United States Patent No. 4,478,853 by Chausse, issued October 23, 1984, relates to a skin conditioner containing a hydroalcohol gel having from about 35 to 50 percent by weight of a lower alkanol, from about 0.1 to 1 percent by weight of a neutralize gelling agent, wherein the gelling agent is a polyacrylic acid cross-linked with a polyether of an oligosaccharide, and from about 1 to 15 percent by weight of a base composition made of a panthenol moisturizer and an emollient such as a polyhydric alcohol humectant and polyether derivative. The viscosity of these compositions are disclosed to range generally from 2,000 to 20,000 cps.

United States Patent No. 3,485,915 by Gerstein et al., issued December 23, 1969, relates to aqueous and/or alcoholic compositions suitable for topical application to the skin containing, as thickening agents, about 0.1 to about 5 percent by weight of a neutralized carboxy polymer and about 0.1 to about 2 percent by weight of hydroxypropyl cellulose.

A product called Avagard, made by 3M, is commercially available having a combination of emulsifiers, namely Beheneth-10, behenyl alcohol, cetylpalmitate, and diisopropyl dimer dilinoleate with 1% chlorhexidine gluconate solution and 61% ethyl alcohol (w/w).

A product called Prevacare, made by Johnson & Johnson, is commercially available having petrolatum as its active ingredient; water as a vehicle; liposome-building blocks including glycerol distearate, stearate-10, cholesterol, and polysorbate 80; sodium laureth sulfate as a sarfactant; propylene glycol as a moisterizer; and preservatives including diazolidinyl urea, methylparaben, and propylparaben. Prevacare-D is a commercially available product having white petrolatum and dimethicone as active ingredients, and also includes cyclomethicone as an emollient; polyethylene and silica as viscosity builders; mineral oil as a moisturizer/emollient, propylparaben as a preservative and fragrance.

A product called Hibiclens, made by Zeneca Pharmaceuticals, is commercially available having 4 percent chlorhexidine gluconate as its active ingredient. Inactive ingredients include fragrance, isopropyl alcohol, purified water, red #40 and other ingredients not specified in its labelling.

A product called Purell, made by GOJO Industries Inc., is commercially available in four formulations. According to the product literature, the active ingredient in each formulation of Purell is 62 percent ethyl alcohol. Inactive ingredients for Purell 2 in 1 are water, Stearyl Alcohol, Cyclomethicone, C12-15 Alkyl Benzoate, Cetyl Lactate, Cocamidopropyl PG-Dimonium Chloride Phosphate, Glycerin, PEG-4, Propylene Glycol, Tocopheryl Acetate, Aminomethyl Propanol, Carbomer, Styrene/ Acrylates Copolymer, Fragrance (Parfum), Diazolidinyl Urea, Iodopropynyl Butylcarbamate, Methylparaben, and Propylparaben; for Purell Original are water, Glycerin, Isopropyl Myristate, Propylene Glycol, Tocopheryl Acetate, Aminomethyl Propanol, Carbomer, and Fragrance (Parfum); for Purell with Aloe are: water, Aloe Barbadensis Leaf Juice, Glycerin, Isopropyl Myristate, Propylene Glycol, Tocopheryl Acetate, Aminomethyl Propanol, Carbomer, Fragrance (Parfum), Blue

1(CI 42090), Yellow 5 (CI 19140); and for Purell Kid's Own are water, Isopropyl Myristate, Propylene Glycol, Aminomethyl Propanol, Carbomer, Fragrance (Parfum), and Red 33.

3. SUMMARY OF THE INVENTION

The present invention relates to antimicrobial compositions comprising synergistic combinations of octoxyglycerin and at least one other antimicrobial agent in formulations which are more effective than prior art compositions without causing increased irritation to the skin of the average user. In certain embodiments, skin irritation may be minimized by low concentrations of antimicrobials and/or the presence of soothing compounds such as zinc. Preferred embodiments of the invention comprise combinations of octoxyglycerin, a quaternary ammonium compound, and at least one other antimicrobial agent. Without being bound to any particular theory, it is hypothesized that the unexpected antimicrobial effectiveness of combinations of octoxyglycerin may result from an enhancement of the permeability of microbes to antimicrobials caused by octoxyglycerin.

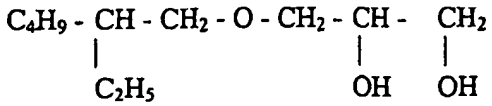
Another aspect of this invention relates to skin friendly hydroalcoholic gel formulations that may be used with the antimicrobial composition described above, with other antimicrobial agents or without the inclusion of any additional antimicrobial agents. It has been discovered that these skin friendly hydroalcoholic gel formulations alone possess an antimicrobial effect and also enhance the rapid and sustained effectiveness of additional antimicrobial agents that are added to the gel. Without being bound to any particular theory, it is hypothesized that the formulations of known compositions interfere with the antimicrobial action of the antimicrobial agents.

4. DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to combinations of octoxyglycerin with at least one, and preferably at least two, antimicrobial agents. In preferred embodiments of the invention such compositions comprise octoxyglycerin and a quaternary ammonium compound.

Octoxyglyerin, as used herein, is also known as glycerol 1-(2-ethylhexyl) ether and is sold under the trade name Sensiva ® SC 50 ("Sensiva®") by

Schulke & Mayr (Rockaway, New Jersey). Octoxyglycerin has the following chemical structure:



which has the empirical formula $C_{11}H_{24}O_3$. The CAS No. of octoxyglycerin is 70445-33-9. Octoxyglycerin has a relative molecular weight of 204.31 g/mol. Sensiva® SC 50 is sold as a clear, almost colorless liquid, having a refractive index of approximately 1.451, a density at 20°C of approximately 0.95 g/ml, a boiling point of >285°C, a flash point of 152°C, a water solubility at 22°C of approximately 1.8 g/l and virtually complete solubility in fat. In addition to having antimicrobial activity, it acts as a mild humectant and skin emollient. The present invention provides for compositions comprising octoxyglycerin at between 1 and 5 percent, and preferably 1-3 percent. It should be noted that all ranges recited herein are inclusive of their limiting values. Sensiva SC50 is essentially pure octoxyglycerin.

Antimicrobial agents which may be used in addition to octoxyglycerin according to the invention include biguanides and phenols. Biguanides may be used in concentrations between about 0.05 and 4 percent and preferably between about 0.05 and 2 percent. Examples of suitable biguanides include polyhexamethylene biguanide (PHMB) at concentrations between about 0.3 and 1 percent, alexidine at concentrations between about 0.05 and 2 percent, and chlorhexidine compounds at concentrations between about 0.05 and 4 percent and preferably between about 0.05 and 1 percent. A chlorhexidine compound, as that term is used herein, includes chlorhexidine free base as well as chlorhexidine salts, including, but not limited to, chlorhexidine diacetate (also known as "chlorhexidine acetate"), chlorhexidine digluconate (also known as "chlorhexidine gluconate"), chlorhexidine palmitate, chlorhexidine diphosphanilate, chlorhexidine dihydrochloride, chlorhexidine dichloride, chlorhexidine dihydroiodide, chlorhexidine diperchlorate, chlorhexidine dinitrate, chlorhexidine sulfate, chlorhexidine sulfite, chlorhexidine thiosulfate, chlorhexidine di-acid phosphate, chlorhexidine difluorophosphate, chlorhexidine diformate, chlorhexidine dipropionate, chlorhexidine di-iodobutyrate, chlorhexidine di-n-valerate, chlorhexidine dicaproate, chlorhexidine malonate, chlorhexidine succinate, chlorhexidine malate, chlorhexidine tartrate, chlorhexidine dimonoglycolate, chlorhexidine monodiglycolate, chlorhexidine dilactate,

chlorhexidine di-alpha-hydroxyisobutyrate, chlorhexidine diglucoheptonate, chlorhexidine di-isothionate, chlorhexidine dibenzoate, chlorhexidine dicinnamate, chlorhexidine dimandelate, chlorhexidine di-isophthalate, chlorhexidine di-2-hydroxynapthoate, and chlorhexidine embonate. Most preferably, the chlorhexidine compound is chlorhexidine digluconate a concentration between 0.05 and 4 percent.

Phenols (phenol derivatives) which may be used according to the invention include, but are not limited to, 2-hydroxyphenol compounds such as triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether, also available as IRGASAN DP300 from Ciba Specialty Chemicals Corp, Greensboro, NC) and 2,2'-dihydroxy-5,5'-dibromo-diphenyl ether; p-nitrophenol, picric acid, xylenol, phenoxyethanol, chlorinated phenols such as parachlorometaxylenol, p-chloro-o-benzylphenol and-dichlorophenol, cresols such as p-chloro-m-cresol, pyrocatechol, resorcinol, 4-n-hexylresorcinol, pryogallol, phloroglucin, carvacrol, thymol, p-chlorothymol, o-phenylphenol, o-benzylphenol, phenol, 4-ethylphenol, 4-phenolsulfonic acids, hexachlorophene, tetrachlorophene, dichlorophene, 2,3-dihydroxy-5,5'-dichlorophenyl sulfide, 2,2'-dihydroxy-3,3',5,5'-tetrachlorodiphenyl sulfide, 2,2'-dihydroxy-3,3',5,5',6,6'-hexachlorodiphenyl sulfide and 3,3'-dibromo-5,5'-dichloro-2,2'-dihydroxydiphenylamine. Preferred is triclosan at a concentration of between about 0.1 and 2 percent and most preferably between about 0.3 and 1 percent. Other phenols may be comprised at concentrations of between about 0.3 and 2 percent, but preferably at concentrations equivalent in potency against *S. aureus* as between 0.3 and 1 percent triclosan.

Additional antimicrobial agents which may be incorporated into compositions of the invention include antifungal agents such as miconazole (preferably at a concentration of 1 - 2 percent), polymixin (preferably at a concentration of 0.3 - 1 percent), neomycin (preferably at a concentration of 0.1 - 0.5 percent), iodine compounds such as povidone iodine (preferably at a concentration of 1 - 10 percent), minocycline (preferably at a concentration of 0.3 – 1.0 percent), and metal salts such as silver sulfadiazine (preferably at a concentration of 1 - 2 percent).

Preferred non-limiting embodiments of the invention comprise octoxyglycerin together with a quaternary ammonium compound, such as, but not limited to, benzalkonium chloride ("BZK", which is particularly preferred),

benzethonium chloride, other benzalkonium or benzethonium halides, including, but not limited to, benzalkonium or benzethonium bromide or fluoride, cetyl pyridinium chloride, dequalinium chloride, N-myristyl-N-methyl-morpholinium methyl sulfate, poly[N-[3-(dimethylammonio)propyl]-N'-[3-(ethyleneoxyethelene dimethylammoinio)propyl]urea dichloride], alpha-4-[1-tris(2-hydroxyethyl)ammonium chloride-2-butenyl]-omega-tris(2-hydroxyethyl)ammonium chloride, poly[oxyethylene (dimethyliminio)ethylene (dimethyliminio)-ethylene dichloride]. The concentrations of quaternary ammonium compound may be between about 0.01 and 0.3 percent; preferably the quaternary ammonium compound is benzalkonium chloride at a concentration between 0.05 and 0.2 percent, more preferably between 0.1 and 0.15 percent.

In certain non-limiting embodiments, compositions of the invention may further comprise one or more alcohol. Alcohols which may be used according to the invention include aliphatic alcohols, including, but not limited, most preferred ethanol or isopropyl alcohol, but also n-propyl alcohol, and mixtures thereof, at concentrations between about 20 and 85 percent and preferably 40 to 70 percent. Suitable alcohols also include fatty alcohols, such as cetyl alcohol, myristyl alcohol, stearyl alcohol, octyl alcohol, decyl alcohol, lauryl alcohol, and combinations thereof, at concentrations between about 0.5 and 5 percent. The present invention further provides for compositions comprising, as at least one alcoholic component, hexanol at a concentration of between three and ten percent and preferably about 5 percent.

The formulations of the invention may further comprise one or more of the following:

A zinc-containing compound such as a zinc salt, including but not limited to zinc gluconate, zinc oxide, zinc stearate, zinc salicylate, zinc carbonate, zinc oleate, zinc acetate, zinc peroxide, zinc phosphate, and zinc undecylenate. Zinc compounds are known to have anti-irritant activity (see, for example, United States Patent No. 5,965,610 by Modak et al. and U.S. Patent No. 5,985,918 by Modak et al., incorporated by reference herein). Preferred zinc compounds for use according to the invention are, for a disinfecting alcohol gel, zinc gluconate and zinc oxide, at concentrations between 0.1 and 1 percent, and preferably 0.8 percent zinc gluconate and 0.2 percent zinc oxide; for an antiseptic aqueous formulation, zinc gluconate and

zinc stearate, at concentrations between 0.2 and 7 percent, and preferably 2.4 percent zinc gluconate and 3.8 percent zinc stearate.

An emollient, which may be, for example, an organic, a hydrocarbon-based or a fatty-ester based emollient. Suitable hydrocarbon-based emollients include petrolatum and mineral oils. Suitable fatty ester based emollients include methyl, isopropyl and butyl esters of fatty acids such as isopropyl palmitate, isopropyl myristate, isopropyl isostearate, isostearyl isostearate, diisopropyl sebacate, and propylene dipelargonate, 2-ethylhexyl isononoate, 2-ethylhexyl stearate, C_{12} - C_{16} fatty alcohol lactates such as cetyl lactate and lauryl lactate, isopropyl lanolate, 2-ethylhexyl salicylate, cetyl myristate, oleyl myristate, oleyl stearate, oleyl oleate, hexyl laurate, and isohexyl laurate. Additional useful emollients include lanolin, olive oil, cocoa butter, and shea butter.

A humectant, such as, for example, glycerine, 1-2-propylene glycol, dipropylene glycol, polyethylene glycol, 1,3-butylene glycol, or 1,2,6-hexanetriol.

A thickening and/or gelling agent, such as, for example, an addition polymer of acrylic acid, a resin such as Carbopol® ETD™ 2020, guar gum, acacia, acrylates/steareth-20 methacrylate copolymer, agar, algin, alginic acid, ammonium acrylate co-polymers, ammonium alginate, ammonium chloride, ammonium sulfate, amylopectin, attapulgite, bentonite, C9-15 alcohols, calcium acetate, calcium alginate, calcium carrageenan, calcium chloride, caprylic alcohol, carbomer 910, carbomer 934, carbomer 934P, carbomer 940, carbomer 941, carboxymethyl hydroxyethyl cellulose, carboxymethyl hydroxypropyl guar, carrageenan, cellulose, cellulose gum, cetearyl alcohol, cetyl alcohol, corn starch, damar, dextrin, dibenzlidine sorbitol, ethylene dihydrogenated tallowamide, ethylene diolamide, ethylene distearamide, gelatin, guar gum, guar hydroxypropyltrimonium chloride, hectorite, hyaluronic acid, hydrated silica, hydroxybutyl methylcellulose, hydroxyethylcellulose, hydroxyethyl ethylcellulose, hydroxyethyl stearamide-MIPA, hydroxypropylcellulose, hydroxypropyl guar, hydroxypropyl methylcellulose, isocetyl alcohol, isostearyl alcohol, karaya gum, kelp, lauryl alcohol, locust bean gum, magnesium aluminium silicate, magnesium silicate, magnesium trisilicate, methoxy PEG-22/dodecyl glycol copolymer, methylcellulose, microcrystalline cellulose, montmorillonite, myristyl alcohol, oat flour, oleyl alcohol, palm kernel alcohol, pectin, PEG-2M, PEG-5M,

polyacrylic acid, polyvinyl alcohol, potassium alginate, potassium aluminium polyacrylate, potassium carrageenan, potassium chloride, potassium sulfate, potato starch, propylene glycol alginate, sodium acrylate/vinyl alcohol copolymer, sodium carboxymethyl dextran, sodium carrageenan, sodium cellulose sulfate, sodium chloride, sodium polymethacylate, sodium silicoaluminate, sodium sulfate, stearalkonium bentotnite, stearalkonium hectorite, stearyl alcohol, tallow alcohol, TEA-hydrochloride, tragacanth gum, tridecyl alcohol, tromethamine magnesium aluminium silicate, wheat flour, wheat starch, xanthan gum, abietyl alcohol, acrylinoleic acid, aluminum behenate, aluminum caprylate, aluminum dilinoleate, aluminum salts, such as distearate, and aluminum isostearates, beeswax, behenamide, behenyl alcohol, butadiene/acrylonitrile copolymer, C29-70 acid, calcium behenate, calcium stearate, candelilla wax, carnauba, ceresin, cholesterol, cholesterol hydroxystearate, coconut alcohol, copal, diglyceryl stearate malate, dihydroabietyl alcohol, dimethyl lauramine oleate, dodecanoic acid/cetearyl alcohol/glycol copolymer, erucamide, ethylcellulose, glyceryl triacetyl hydroxystearate, glyceryl tri-acetyl ricinolate, glycol dibehenate, glycol di-octanoate, glycol distearate, hexanediol distearate, hydrogenated C6-14 olefin polymers, hydrogenated castor oil, hydrogenated cottonseed oil, hydrogenated lard, hydrogenated menhaden oil, hydrogenated palm kernel glycerides, hydrogenated palm kernel oil, hydrogenated palm oil, hydrogenated polyisobutene, hydrogenated soybean oil, hydrogenated tallow amide, hydrogenated tallow glyceride, hydrogenated vegetable glyceride, hydrogenated vegetable oil, Japan wax, jojoba wax, lanolin alcohol, shea butter, lauramide, methyl dehydroabietate, methyl hydrogenated rosinate, methyl rosinate, methylstyrene/vinyltoluene copolymer, microcrystalline wax, montan acid wax, montan wax, myristyleicosanol, myristyloctadecanol, octadecene/maleic anhyrdine copolymer, octyldodecyl stearoyl stearate, oleamide, oleostearine, ouricury wax, oxidized polyethylene, ozokerite, paraffin, pentaerythrityl hydrogenated rosinate, pentaerythrityl tetraoctanoate, pentaerythrityl rosinate, pentaerythrityl tetraabietate, pentaerythrityl tetrabehenate, pentaerythrityl tetraoleate, pentaerythrityl tetrastearate, ophthalmic anhydride/glycerine/glycidyl decanoate copolymer, ophthalmic/trimellitic/glycols copolymer, polybutene, polybutylene terephthalate, polydipentene, polyethylene, polyisobutene, polyisoprene, polyvinyl butyral, polyvinyl laurate, propylene glycol dicaprylate, propylene glycol dicocoate, propylene glycol diisononanoate, propylene glycol dilaurate, propylene glycol dipelargonate,

propylene glycol distearate, propylene glycol diundecanoate, PVP/eiconsene copolymer, PVP/hexadecene copolymer, rice bran wax, stearlkonium bentonite, stearalkonium hectorite, stearamide, stearamide DEA-distearate, stearamide DIBA-stearate, stearamide MEA-stearate, stearone, stearyl alcohol, stearyl erucamide, stearyl stearate, stearyl stearoyl stearate, synthetic beeswax, synthetic wax, trihydroxystearin, triisononanoin, triisostearin, tri-isostearyl trilinoleate, trilaurin, trilinoleic acid, trilinolein, trimyristin, triolein, tripalmitin, tristearin, zinc laurate, zinc myristate, zinc neodecanoate, zinc rosinate, and mixtures thereof.

A neutralizing agent, which may be included, for example, to neutralize carboxyl groups present in one or more other component, such as carboxyl groups in a thickening agent. Suitable neutralizing agents include diisopropylamine and triethanolamine.

A surfactant, which may be an anionic surfactant, a cationic surfactant, an ampholytic surfactant, or a nonionic surfactant, such as, for example, nonionic surfactants such as polyethoxylates, fatty alcohols (*e.g.*, ceteth-20 (a cetyl ether of polyethylene oxide having an average of about 20 ethylene oxide units) and other "BRIJ"® nonionic surfactants available from ICI Americas, Inc. (Wilmington, DE)), cocamidopropyl betaine, alkyl phenols, fatty acid esters of sorbitol, sorbitan, or polyoxyethylene sorbitan. Suitable anionic surfactants include ammonium lauryl sulfate and lauryl ether sulfosuccinate. A preferred surfactant is lauroyl ethylenediamine triacetic acid sodium salt at a concentration between about 0.5 - 2.0%. Suitable concentrations of surfactant are between about 0.05 and 2 percent.

Water used in the formulations is preferably deionized water having a neutral pH.

Additional additives, including but not limited to a silicone fluid (such as dimethicone or cyclomethicone), dyes, fragrances, etc. Examples of additional additives include but are not limited to: pH adjusters, including basic pH adjusters such as ammonia, mono-, di- and tri- alkyl amines, mono-, di- and tri-alkanolamines, alkali metal and alkaline earth metal hydroxides (*e.g.*, ammonia, sodium hydroxide, potassium hydroxide, lithium hydroxide, monoethanolamine, triethylamine, isopropylamine, diethanolamine and triethanolamine); acid pH adjusters such as

mineral acids and polycarboxylic acids (*e.g.*, hydrochloric acid, nitric acid, phosphoric acid, sulfuric acid, citric acid, glycolic acid, and lactic acid); vitamins such as vitamin A, vitamin E and vitamin C; polyamino acids and salts, such as ethylenediamine tetraacidic acid (EDTA), preservatives such as Germall Plus and DMDM hydantoin, and sunscreens such as aminobenzoic acid, arobenzone, cinoxate, diioxybenzone, homosalate, menthyl anthranilate, octocrylene, octyl methoxycinnamate, octyl salicylate, oxybenzoate, padimate O, phenylbenzimidazole, sulfonic acid, sulisobenzone, titanium dioxide, trolamine salicylate and zinc oxide.

The present invention further relates to hydroalcoholic gel compositions comprising combinations of one percent or less of hydrogel dissolved in water at ambient temperature and three percent or less of emollient dissolved in alcohol or three percent or less of emulsifier wherein said compositions have viocosities below 4000 centipoises at between 20 and 40 °C. These percentages and further percentages discussing these hydroalcoholic gel compositions should be considered weight/weight percentages, unless specified otherwise. In preferred embodiments of the invention such compositions comprise 30 to 80 percent alcohol, 15 to 70 percent water, 0.05 to 0.5 percent hydrogel and 0.2 to 3.0 percent emollient and/or 0.05 to 0.5 percent emulsifier with viscosities of less than 2000 cps, most preferably between 50-500 cps. Additional embodiments of this invention further include silicone polymer, emollient solvent, antimicrobial agent, and thickening agent, while maintaining the low viscosities as preferred.

A hydrogel, as used herein, includes hydroxypropylmethyl cellulose, cationic hydroxyethyl cellulose (U-care polymers), ethyl cellulose, hydroxypropyl cellulose, hydroxymethyl cellulose, carboxy methyl cellulose, polyethylene oxide (polyox resins), and chitosan pyrrolidone carboxylate (Kytomer PC). These hydrogels preferably do not bind to any added antimicrobial agent, therefore leaving the optionally added antimicrobial agent free for rapid and long-term activity. In addition, it has been discovered that alcohol used to form the hydroalcoholic gel is not trapped in the hydroalcoholic gel composition and is therefore available for rapid and long-term action. The hydrogel is present in a concentration between 0.1 and 1.0 percent, and preferably is a cationic hydroxyethyl cellulose (U-care polymers) in a concentration between 0.05 and 0.5 percent, most preferably 0.2 percent.

Alcohols that may be used according to this invention relating to hydroalcoholic gel compositions include the alcohols discussed above, preferably aliphatic alcohols, including, but not limited to, ethenol, isopropyl alcohol, n-propyl alcohol, and mixtures thereof; fatty alcohols, including, but not limited to, cetyl alcohol, myristol alcohol, stearyl alcohol, octyl alcohol, decyl alcohol and lauryl alcohol, and mixtures thereof; and hexanol. The concentration of alcohol may be between 30 and 95 percent, preferably between 40 and 70 percent; preferably the aliphitic alcohols is ethanol or isopropyl alcohol at a concentration between and 60 and 95 percent; when present, the concentration of fatty alcohols is preferably between 0.5 and 5.0 percent; and, when present, the concentration of hexanol is preferably between 3 and 10 percent, more preferably 5 percent.

Water, when used in these hydroalcoholic gel compositions, is preferably deionized water having a neutral pH. The present invention provides for compositions comprising water at between 15 and 70 percent. The concentration of water should be suitable to dissolve the hydrogels according to the invention.

An emollient and/or humectant (collectively referred to hereinafter as emollients), as used according to this invention relating to hydroalcoholic gel compositions, include the emollients and humectants discussed above, and preferably include one or more than one PEG 20 Almond Glycerides, Probutyl DB-10, Glucam P20, Glucam E-10, Glucam P-10, Glucam E-20, Glucam P-20 distearate, glycerin, propylene glycol, octoxy glycerin (Sensiva), cetyl acetate and acetylated lanolin alcohol (Acetulan), cetyl ether (PPG-10), myristyil ether (PPG-3), hydroxylated milk glycerdcs (Cremerol HMG) , polyquaternium compounds (U-care compounds), chitosn (Kytamer), copolymer of dimethyl dialyl ammonium chloride and acrylic acid (Merquat), dipropylene glycol methyl ethers (Dowanol DPM Dow Corning), and polypropylene glycol ethers (Ucon 50-HB-660, Union Carbide). Preferably the emollient is present at a concentration of three percent or less, such that the viscosity of the composition is preferably less than 2000 centipoise at 20 to 40 °C, more prefcrably between 0.2 and 3 percent.

Surfactants and/or emulsifiers (collectively referred to hereinafter as emulsifiers), as used according to this invention relating to hydroalcoholic gel compositions, include the emulsifiers and surfactants discussed above, and preferably

include non-ionic or cationic self-emulsifying waxes that are preferably soluble in alcohol at ambient temperature including Incroquat Behenyl TMS, Incroquat Behenyl TMS-50, Polawax, stearyl alcohol and cetearyl alcohol. These emulsifiers are present at a concentration between 0.05 and 3.0 percent. Emulsifiers to this invention preferably include Incroquat Behenyl TMS, which is a mild cationic emulsifier as well as an excellent conditioner, and Polawax, which is a non-ionic self emulsifying wax, individually at a concentration of between 0.05 and 0.5 percent, and incombination at a concentration of between 0.05 and 0.5 percent, more preferably in combination at a concentration ratio of approximately 1:1. If more than one emulsifier is used, it is preferred that the total concentration of all of the emulsifier is between 0.05 and 0.5 percent of the total concentration.

Silicone polymer, as used according to this invention relating to hydroalcoholic gel compositions, includes the silicone polymers discussed above, and preferably includes one or more than one polydimethylsiloxane polymer (Dow Corning 225 Silicone Fluid), dimethiconol fluid in dimethicone (Dow Corning 1403 Silicone Fluid), cyclomethicone and dimethicone copolyl (Dow Corning 3225C Silicone Fluid), and silicone glycol (BASF 1066 DCG polyol). Suitable concentrations of silicone polymer are between about 0.1 and 1.0 percent.

Emollient solvents include, but are not limited to, one or more than one glycidyl ethers having alkyl chains up to and including 18 carbon molecules and ethoxylates and propoxylates thereof, glyceryl ethers having alkyl chains up to and including 18 carbon molecules and ethoxylates and propoxylates thereof, mono- and diglyceryl ethers having alkyl chains up to and including 18 carbon molecules and ethoxylates and propoxylates thereof, ethoxylate and propoxylate ethers, ethoxy diglycol esters, ethyl hexyl alcohol propoxylate, and propylene glycol esther ethoxylates and propoxylates, and preferably Arlamol (Altas). Suitable concentrations of emollient solvent are between 0.5 and 5 percent.

Thickening agents that may be used according to this invention relating to hydroalcoholic gel compositions include the thickening agents and gelling agents discussed above, preferably behenyl alcohol, crodamol, and crothix. Suitable concentration of thickening agent are between 0.05 and 1.0 percent. Gelling agents

such as Caropol are not preferred due to their high viscosity and their requiring neutralizing agents to neutralize the gelling agent with alkaline materials.

Antimicrobial agents that may be used in addition to the hydroalcoholic gel composition according to the invention include the antimicrobial agents discussed above, including, but not limited to, one or more than one biguanides, phenols, quaternary ammonium compounds and anti-fungal agents. Preferred concentrations are provided above. Preferably, the concentration of the one or more that one antimicrobial agent is less than three percent. More than one antimicrobial agents may be used in combination, such as chlorhexidine gluconate, benzalkonium chloride and phenoxy ethanol, preferably at a concentration of between 0.05 and 0.5 percent, 0.1 and 0.25 percent, and 0.1 and 1.0 percent, respectively. Because cationic antimicrobials, such as biguanides and quaternary ammonium compounds, can bind to the surface of the skin, they may not be available to inactivate pathogens that come into contact with the skin. The gel formulation according to the invention forms a film on the surface of the hand when applied, which film acts as a barrier preventing the antimicrobial agents that may be added to the gel from binding to the surface of the skin.

Ambient temperature is defined herein between 20 and 35 °C. Room temperature is defined herein between 20 and 25 °C.

Specific, non-limiting embodiments of the invention include the following compositions, which may further comprise additional ingredients that do not substantially effect the antimicrobial properties of the composition. For the following formulations, the water indicated was added last to the other ingredients to bring the total volume to 100 percent. For specific embodiments numbers 11-23, all percentages should be considered weight/weight percentages, unless specified otherwise.

1. An antiseptic alcohol gel comprising:

zinc gluconate	0.8 percent
zinc oxide	0.2 percent
ethyl alcohol (volume/volume)	65.0 percent

hydroxy methyl propyl cellulose (K100M)	0.3 percent
U-care JR 400 (polyquaternium-10) (Amerchol Corp.)	0.15 percent
Incroquat Behenyl TMS (Croda, Inc.)	1.0 percent
Polawax A-31 (Croda, Inc.)	1.0 percent
stearyl alcohol - Crodacol(S70) (Croda, Inc.)	1.0 percent
Cremerol HMG (Amerchol Corp.)	1.0 percent
dimethicone (volume/volume)	0.5 percent
Germall plus (ISP Sutton Laboratories)	0.25 percent
propylene glycol (volume/volume)	1.5 percent
glycerin (volume/volume)	1.0 percent
water (volume/volume)	23.13 percent
chlorhexidine digluconate	0.05 percent
phenoxyethanol	1.0 percent
BZK	0.12 percent
Sensiva SC50 (volume/volume)	2 percent

where the gel may be applied to and rubbed over the skin to achieve its antimicrobial effect.

2. An antiseptic alcohol gel comprising:

water (volume/volume)	31.32 percent
U-care	0.08 percent

(Amerchol Corp.)	
hydroxypropylmethylcellulose (K-100) (Dow Corning)	0.15 percent
Polyox WSR 301 (polyethyleneoxide) (Dow Corning)	0.03 percent
Incroquat (Croda, Inc.)	0.4 percent
Polawax A-31 (Croda, Inc.)	0.4 percent
polyethylene glycol	0.25 percent
ethanol (volume/volume)	63.5 percent
Glucam E-20 (Amerchol Corp.)	0.4 percent
Silicone 225 (volume/volume) (Dow Corning)	0.1 percent
Sensiva SC50 (volume/volume)	2.0 percent
phenoxyethanol	1.0 percent
chlorhexidine digluconate	0.05 percent
BZK	0.12 percent
Germall Plus (Sutton Laboratories)	0.2 percent

3. An antiseptic aqueous formulation comprising:

zinc gluconate	2.4 percent
zinc stearate	3.8 percent
hydroxy methyl propyl cellulose (K100M)	0.5 percent
Kytamer PC (Chitisan) (Amerchol Corp.)	0.15 percent

U-care JR 400 (Amerchol Corp.)	0.1 percent
Incroquat behenyl TMS (Croda, Inc.)	1.0 percent
Crodamol NM (Croda, Inc.)	1.6 percent
Acetulan (Amerchol Corp.)	2.0 percent
Cremerol HMG (Amerchol Corp.)	1.0 percent
stearyl alcohol	2.0 percent
allantoin	0.25 percent
Germall Plus (ISP Sutton Laboratories)	0.3 percent
dimethicone (volume/volume)	1.0 percent
water (volume/volume)	81.48 percent
PHMB	0.3 percent
phenoxyethanol	1.0 percent
BZK	0.12 percent
Sensiva SC50 (volume/volume)	2 percent

4. An antimicrobial scrub gel comprising:

water	30.5 percent
U-care (Amerchol Corp.)	0.1 percent
hydroxy propyl methyl cellulose (K100) (Dow Corning)	0.2 percent
Polyox WSR 301 (polyethyleneoxide) (Dow Corning)	0.1 percent

Incroquat (Croda, Inc.)	0.4 percent
Polawax A-31 (Croda, Inc.)	0.4 percent
propylene glycol	1.0 percent
ethanol (volume/volume)	63.5 percent
Glucam E-20 (Amerchol Corp.)	0.4 percent
Masil SF 19 CG surfactant	1.0 percent
phenoxyethanol	1.0 percent
Sensiva SC50 (volume/volume)	1.0 percent
chlorhexidine digluconate	0.05 percent
BZK	0.12 percent
Germall Plus (Sutton Laboratories)	0.2 percent

5. An antimicrobial scrub gel, for example for pre-operative skin disinfection, comprising:

ethanol (volume/volume)	35 percent
isopropanol (volume/volume)	35 percent
zinc gluconate	0.5 percent
zinc oxide	0.2 percent
hydroxy methyl propyl cellulose (K100M)	0.3 percent
Germall Plus (ISP Sutton Laboratories)	0.25 percent
hexanol (volume/volume)	5.0 percent
PXE	1.0 percent

Sensiva (volume/volume)	1.5 percent
chlorhexidine digluconate	0.05 percent

with water added to 100 percent (approximately 21.2 milliliters/100 ml solution).

6. Another antimicrobial scrub gel, for example for pre-operative skin disinfection, comprising:

water (volume/volume)	23.28 percent
Polyox WSR 205	0.2 percent
U-care JR 400	0.2 percent
ethanol (95%) (volume/volume)	65 percent
propylene glycol	3 percent
Sensiva SC50 (volume/volume)	2 percent
BZK	0.12 percent
phenoxyethanol	1.0 percent
povidone iodine	5.0 percent
Germall Plus	0.2 percent

7. An antimicrobial soap comprising:

water (volume/volume)	51.2 percent
U-care (Amerchol Corp.)	0.1 percent
hydroxy propyl methyl cellulose (K-100) (Dow Corning)	0.2 percent
Polyox WSR 301 (polyethyleneoxide)	0.03 percent
ethanol (volume/volume)	40 percent

Pluronic F-87 (BASF)	2.0 percent
Masil SF 19 CG surfactant	1.0 percent
Cocamidopropyl betaine (Witco Corp.)	2.0 percent
propylene glycol	1.0 percent
phenoxyethanol	1.0 percent
chlorhexidine digluconate	0.05 percent
BZK	0.12 percent
Sensiva SC50 (volume/volume)	0.5 percent
Germall Plus (Sutton Laboratories)	0.2 percent

8. An antifungal cream comprising miconazole (1-2 percent), chlorhexidine digluconate (0.05 - 0.2 percent), and Sensiva SC50(1-3 percent) in a hydrophilic cream base.

9. A topical antiseptic ointment for wound care comprising polymixin (0.3 - 1%), neomycin (0.1 - 0.5 percent), chlorhexidine digluconate (0.05 - 0.2 percent), and Sensiva SC50(1 - 3 percent) in a hydrophilic base.

10. A topical antiseptic ointment for burn wound care comprising silver sulfadiazine (1 - 2 percent), chlorhexidine digluconate (0.05 - 0.2 percent) and Sensiva SC50 (1 - 3 percent) in a hydrophilic base.

11. A hydroalcoholic disinfectant gel comprising:

Water	30.6
Polyquaternium-10 (U-careJR30)	0.2
Kytamer L	0.1
Ethanol	65
Incroquat behenyl TMS	0.8
Polowax A31	0.4
Octoxy Glycerin	2

Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5
Silicone Glycol (BASF 1066-DCG Polyol)	0.2

12. A hydroalcoholic disinfectant gel comprising:

Water	30.6
Polyquaternium-10 (U-care JR30)	0.2
Kytamer L	0.1
Ethanol	65
Incroquat behenyl TMS	0.8
Polowax A31	0.4
Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5
Silicone Glycol (BASF 1066-DCG Polyol)	0.2

13. A hydroalcoholic disinfectant gel comprising:

Water	30.6
Hydroxy propyl methyl cellulose (K 100)	0.2
Kytamer L	0.1
Ethanol	65
Incroquat behenyl TMS	0.8
Polowax A31	0.4
Octoxy Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5
Silicone Glycol (BASF 1066-DCG Polyol)	0.2

14. A hydroalcoholic disinfectant gel comprising:

Water	30.6
Hydroxy propyl methyl cellulose (K 100)	0.2
Kytamer L	0.1

Ethanol	65
Incroquat behenyl TMS	0.8
Polowax A31	0.4
Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5
Silicone Glycol (BASF 1066-DCG Polyol)	0.2

15. A hydroalcoholic surgical scrub comprising:

Water	26.8
U care JR30	0.3
Ethanol	70
Octoxy Glycerin	2
Silicone Glycol (BASF 1066-DCG Polyol)	0.2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

16. A hydroalcoholic surgical scrub comprising:

Water	26.8
U care JR30	0.3
Ethanol	70
Glycerin	2
Silicone Glycol (BASF 1066-DCG Polyol)	0.2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

17. A hydroalcoholic antimicrobial scrub, for example for pre-operative skin disinfection, comprising:

Water	26.8
U care JR30	0.3
Isopropanol	70

Octoxy Glycerin	2
Silicone Glycol (BASF 1066-DCG Polyol)	0.2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

18. A hydroalcoholic antimicrobial scrub, for example for pre-operative skin disinfection, comprising:

Water	24.8
U care JR30	0.3
Ethanol	62
Octoxy Glycerin	2
Silicone Glycol (BASF 1066-DCG Polyol)	0.2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5
Povidone Iodine	10

19. A hydroalcoholic antimicrobial soap comprising:

Ethanol	52
Pluronic F-87	2
Masil SF19(Silicone surfactant)	1
Masil 1066	1
Cocamidopropyl betaine	1
Mirapol A-15	1
Water	35.5
U-care JR30	0.1
Polyox WOR-205	0.2
Germall Plus	0.2
CHG	0.05
BZK	0.12
Propylene glycol	2
Glycerin	2
Octoxy glycerin	1

Phenoxyethanol	0.5

20. A hydroalcoholic disinfectant gel comprising:

Water	31.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Incroquat behenyl TMS	0.4
Octoxy Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

21. A hydroalcoholic disinfectant gel comprising:

Water	31.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Incroquat behenyl TMS	0.4
Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

22. A hydroalcoholic disinfectant gel comprising:

Water	33.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Isopropanol	5
Incroquat behenyl TMS	0.4
Octoxy Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

23. A hydroalcoholic disinfectant gel comprising:

Water	26.73

Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Isopropanol	5
Incroquat behenyl TMS	0.4
Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

5. EXAMPLES

EXAMPLE 1 : SENSIVA + BZK

Sensiva SC50 and/or benzalkonium chloride ("BZK") were added, in various concentrations, to the following alcohol gel base:

ethyl alcohol (volume/volume)	65 percent
hydroxy methyl propyl cellulose (K100M)	0.3 percent
hydroxy propyl cellulose (HF) (volume/volume)	0.1 percent
Glucam P20 (volume/volume)	1.0 percent
Glucam P20 distearate (volume/volume)	1.5 percent
U-care JR 400 (polyquaternium-10)	0.15 percent
silicone (DC 1403) (volume/volume)	1.5 percent
Germall Plus	0.25 percent

to which water was added, after the incorporation of other additives, to bring the total volume to 100 percent (typically requiring approximately 20-30 percent (volume/volume)). The amount of Sensiva, throughout the example section, is a volume/volume percentage.

Antimicrobial activity was evaluated using the following assay. 1 milliliter of 10^8 colony-forming units ("cfus") of test organism per milliliter was added to 1 milliliter of bovine adult serum in a sterile culture tube and mixed. 1

milliliter of the test gel was added to each tube, and was vortexed to mix. After 15 seconds, three 0.5 ml aliquots were removed and further diluted 1:1000 with LTSB (lecithin-containing trypticase soy broth) drug-inactivating medium, and, of the resulting liquid, 0.5 milliliters were plated on each trypticase soy agar ("TSA") plate. The resulting plates were incubated at 37° C for 24 hours and the colony count per tube was determined.

The foregoing method was used to determine the antimicrobial activities of formulations of the above alcohol gel base comprising either Sensiva SC50, BZK or combinations of Sensiva SC50 and BZK. The results for Sensiva SC50 used alone are shown in Table 1, and the results for Sensiva SC50, BZK and Sensiva SC50/BZK combinations are shown in Table 2.

TABLE 1

% Sensiva	0	0.5	1.0	2.0	3.0	5.0
S. aureus (cfu/tube)	1×10^8	1×10^7	4×10^7	3×10^6	1×10^6	1×10^6
fold-reduction*	-	2.5	9	33	100	100

*relative to control

TABLE 2

% Sensiva	0	1.0	2.0	0	0	0	1.0	1.0	2.0	2.
% BZK	0	0	0	0.12	0.19	0.5	0.12	0.19	0.12	0.1
S. aureus (cfu/tube)	1×10^8	4×10^7	3×10^6	1.6×10^7	2×10^7	3.7×10^6	8×10^5	2×10^4	8×10^3	3.0 10
Log 10 cfu reduction relative to control	-	1	1.5	0.8	0.7	1.4	2.1	3.7	4.1	4.
Increase in log 10 beyond additive effect	NA	NA	NA	NA	NA	NA	0.3	2	1.8	2.
fold reduction relative to control	-	10	33	6.25	5	27	125	5×10^3	1.25×10^4	3.3 10

Tables 1 and 2 show that no significant antimicrobial activity against *S. aureus* was obtained with 2-5 percent Sensiva; the antimicrobial activity was not significantly different between 2, 3 and 5 percent of Sensiva. Similarly, 0.12 and 0.19

percent BZK exhibited minimal or no antimicrobial activity (Table 2). However, combinations of 1-2 percent Sensiva SC50 and 0.12-0.19 percent BZK showed 5000-33000 fold reduction in colony-forming units compared to control values (Table 2).

EXAMPLE 2 : SENSIVA + CHLORHEXIDINE DIGLUCONATE

Assays using the same gel base and protocol as set forth in Example 1 to test activities of Sensiva, chlorhexidine digluconate ("CHG"), and combinations thereof gave the following results, shown in Table 3.

TABLE 3

% Sensiva	0	0	0	0	1.0	1.0	1.0	2.0	2.0	2.
% CHG	0	0.05	0.25	0.5	0.05	0.25	0.5	0.05	0.25	0.
S. aureus (cfu/tube)	1×10^8	1.1×10^7	8×10^6	4.2×10^6	1.2×10^5	6×10^4	8×10^3	8×10^3	5×10^3	1 x
Log 10 cfu reduction relative to control	-	1.0	1.1	1.4	2.9	3.1	4.1	4.1	4.3	4.
Increase in log 10 beyond additive effect	NA	NA	NA	NA	0.4	1.1	1.7	1.6	1.7	2.
fold reduction relative to control	-	9	12.5	23.8	833	1666	12500	12500	20000	1 x

Thus, Sensiva SC50 (1-2 percent) and CHG (0.05-0.5 percent) used individually showed 9-35 fold reduction in colony counts as compared to control, whereas a combination of 1-2 percent Sensiva with 0.05-0.5 percent CHG showed 800-100,000 fold reduction. Thus, the combination of Sensiva and CHG appears to be synergistic. When benzalkonium chloride was added to formulation, the antimicrobial activity was improved still further, as shown in the following example section.

EXAMPLE 3 : SENSIVA + CHLORHEXIDINE DIGLUCONATE + BZK

Assays using the same gel base and protocol as set forth in Example 1 to test activities of combinations of Sensiva, chlorhexidine digluconate ("CHG") and BZK gave the following results, shown in Table 4.

TABLE 4

% Sensiva	0	0	1.0	2.0
% BZK	0	0.12	0.12	0.12
% CHG	0	0.05	0.05	0.05
Growth (cfu/ml)	1×10^8	1.2×10^7	4×10^4	0
Log 10 cfu reduction relative to control	0	1.0	4.0	8.0
Increase in log 10 beyond additive effect	NA	NA	2.1	5.1
fold reduction relative to control	-	8.3	2500	10^8

NA = not applicable

EXAMPLE 4: COMBINATIONS OF SENSIVA AND OTHER ANTIMICROBIALS

Since Sensiva does not exhibit potent microbicidal activity even at concentrations of between 3 and 5 percent, it is surprising that this compound exhibits synergism with chlorhexidine digluconate and BZK. Octoxyglycerin (Sensiva) has been reported to have the property of deeper penetration into the upper layers of the epidermis. Without being bound by any particular theory, the mechanism of synergistic action may be explained as follows. When a bacterium is exposed to Sensiva and a second antimicrobial agent, Sensiva may penetrate through the bacterial cell wall and thereby compromise the bacterial transport system. This may result in increased uptake of the second antimicrobial agent. This mechanism would indicate that Sensiva would promote the antimicrobial effects of a diverse array of compounds, including quaternary ammonium compounds, biguanides, chlorinated phenols, metal salts, antifungal azoles, etc.

Accordingly, the antimicrobial activity of various combinations of Sensiva and other antimicrobials was tested, using concentrations that fall within the recommended usage range for topical formulations. The following agents were tested. Benzalkonium chloride (BZK) and benzethonium chloride (BZT) were tested as representative of the class of quaternary ammonium compounds. Chlorhexidine digluconate (CHG) and polyhexamethylene biguanide (PHMB) were tested as

representative of the class of biguanides. Parachlorometaxylenol (PCMX) and triclosan (TC)were tested as representative of the class of chlorinated phenols. Povidone iodine (PVI) was tested as representative of the class of iodine compounds. Silver sulfadiazine (AgSD) was tested as representative of the class of metal salts. Neomycin and miconazole were tested as representative of the class of antibiotics. The alcohol gel base and protocol set forth in Example 1 were used to produce the data set forth in Table 5.

Similar protocols were then used to test the antibacterial activity of Sensiva combined with chorhexidine digluconate and another antimicrobial agent. The results are shown in Table 6.

TABLE 5

% Antimicrobial	% Sensiva	Growth (CFU/ml)	fold reduction*
0 Control	0	1×10^8	-
0	2.0	3×10^6	33
BZK			
0.12	0	1.6×10^7	6.25
0.12	2.0	8.0×10^3	12500
BZT			
0.12	0	1.0×10^7	10
0.12	2.0	5.0×10^3	20,000
CHG			
0.05	0	1.1×10^7	9
0.05	2.0	8.0×10^3	12,500
PHMB			
0.3	0	3.0×10^6	33
0.3	2.0	4.0×10^3	25,000
TC			
0.3	0	1.0×10^8	0
0.3	2.0	2.2×10^5	450
PCMX			
0.3	0	1.0×10^8	0
0.3	2.0	6.2×10^4	1612
AgSD			
1.0	0	1.0×10^8	0
1.0	2.0	3.0×10^5	330
PVI			
1.0	0	2.0×10^7	5
1.0	2.0	3.0×10^4	3,333
Neomycin			
0.3	0	2.3×10^7	4.3
0.3	2.0	1.0×10^3	100,000
Miconazole			
1.0	0	1.0×10^8	0
1.0	2.0	6.0×10^4	1666

*relative to control

TABLE 6

% Antimicrobial	% Sensiva	%CHG	Growth (CFU/ML)	Fold Reduction Compared to Control
0	0	0	1.0×10^8	-
0	2.0	0	3.0×10^6	33
0	2.0	0.05	8.0×10^3	12,500
BZK				
0.12	0	0.05	1.2×10^7	8.3
0.12	2.0	0.05	0	10^8
TC				
0.3	0	0.05	9.0×10^6	11.1
0.3	2.0	0.05	0	10^8
PCMX				
0.3	0	0.05	7.0×10^6	14.2
0.3	2.0	0.05	0	10^8
AgSD				
1.0	0	0.05	1.0×10^7	10
1.0	2.0	0.05	0	10^8
PVI				
1.0	0	0.05	1.0×10^7	10
1.0	2.0	0.05	0	10^8
Neomycin				
0.3	0	0.05	1.0×10^6	100
0.3	2.0	0.05	0	10^8

The data shown in Table 5 indicate that Sensiva, at a concentration of 2.0 percent, produced a 33-fold reduction in bacterial colony formation, and the antibacterial activity of the other antimicrobials tested, used alone, was less than or equal to 33-fold. Combination of these antimicrobials with Sensiva greatly resulted in an antibacterial activity greater than what would have been expected, based on the inhibitory activity of either agent used separately. The extent of this enhancement varied among antimicrobials; for example, the activity of quaternary ammonium compounds, used in combination with Sensiva, was observed to be 12,500 and 20,000-fold greater than control. The biguanides chlorhexidine digluconate and parahexamethylenebiguanide, in combination with Sensiva, produced an antimicrobial activity 12,500 and 25,000-fold greater, respectively, than control. Neomycin, in combination with Sensiva, exhibited an antimibrobial activity 100,000 greater than control. Thus, Sensiva has been demonstrated to enhance the antimicrobial effects of a wide variety of agents. The data shown in Table 6 further

show that combinations of Sensiva and chlorhexidine digluconate with various antimicrobials exhibit a further enhancement in activity.

EXAMPLE 5: ADDITIONAL DATA

Assays using the same gel base and protocol as set forth in Example 1 to test activities of combinations of Sensiva and other antimicrobials gave the following results, shown in Table 7.

TABLE 7

Agent(s)	Concentrations	Growth (cfu/tube)
control (without gel base)	-	$2.5 - 4.2 \times 10^8$
Sensiva	0.5	4.0×10^7
Sensiva	1.0	1.0×10^7
BZK	0.019	8.0×10^7
BZK + Sensiva	0.019 1.0	2.0×10^7
BZK + Sensiva	0.019 2.0	1.2×10^7
BZK	0.12	1.6×10^7
BZK + Sensiva	0.12 0.5	1.4×10^7
BZK + Sensiva	0.12 1.0	8.0×10^5
CHG	0.05	1.1×10^7
CHG + Sensiva	0.05 0.5	6.3×10^6
CHG + Sensiva	0.05 1.0	1.2×10^5
PCMX	0.15	3.5×10^8
PCMX + Sensiva	0.15 2.0	4.1×10^5
TC + BZK	0.3 0.12	1.0×10^7
TC + BZK + Sensiva	0.3 0.12 2.0	4.0×10^3
PCMX + BZK	0.3 0.12	2.0×10^6
PCMX + BZK + Sensiva	0.3 0.12 2.0	1.0×10^3
Miconazole + CHG	1.0 0.05	1.0×10^7
Miconazole + CHG + Sensiva	1.0 0.05 2.0	1.0×10^3
PVI + CHG	1.0 0.05	1.0×10^7
PVI + CHG + Sensiva	1.0 0.05 2.0	0

EXAMPLE 6: COMBINATIONS OF SENSIVA, BZK, AND OTHER AGENTS

Again using the alcohol gel base and protocol described in Example 1, various combinations of Sensiva, the quaternary ammonium compound BZK, and other antimicrobials produced the results shown in Table 8.

TABLE 8

Agent(s)	Concentration (%)	Growth (cfu/tube)
Control (no gel base)	-	2.0×10^8
Control (gel base)	-	1.2×10^8
PXE	1.0	1.0×10^8
PXE + Sensiva	1.0 1.0	2.0×10^7
PXE + Sensiva	1.0 2.0	3.3×10^5
BZK + CHG + Sensiva	0.12 0.05 1.0	4.0×10^4
BZK + CHG + Sensiva	0.12 0.05 2.0	0
BZK + CHG + Sensiva + PXE	0.12 0.05 1.0 1.0	0
BZK + PHMB + Sensiva	0.12 0.3 1.0	8.0×10^3
BZK + PHMB + Sensiva + PXE	0.12 0.3 1.0 1.0	0

The above data demonstrates that the addition of the phenol derivative, phenoxyethanol, enhanced the antimicrobial activity of several combinations of Sensiva and other antimicrobials.

EXAMPLE 7: SUSTAINED ACTIVITY OF ANTIMICROBIAL PREPARATIONS

Natural leather was cut into 2 x 2 cm pieces, washed, and sterilized. For each test group 4 pieces were used. Equal amounts (0.25 ml) of various test formulations were applied uniformly on the surface of each piece, and then allowed to dry for 3 hours. Then 10 microliters of a *Staphylococcus aureus* culture (10^7

CFU/ml) was spread uniformly on the surface of the treated leather patches. After 1 minute, the inoculated side of the leather was rinsed with 10 ml of drug-inactivating medium (LTSB), of which a 0.5 ml aliquot was plated on the surface of a D/E (drug-inactivating) plate. Plates prepared in this manner were incubated for 24 hours at 37°C and bacterial colonies were counted. The results, which demonstrate sustained antimicrobial activity of the Sensiva formulations, are shown in Table 9.

TABLE 9

Group	*Staphylococcus aureus* CFU/patch
0.12% BZK + 0.5% PXE + 0.05% CHG + 1.0% Sensiva	30
0.12% BZK + 0.5% PXE + 0.3% PHMB + 1.0% Sensiva	20
Prevacare	1.3×10^4
Gel Base (control)	1.1×10^4
Control	1.2×10^5

EXAMPLE 8: AQUEOUS SENSIVA FORMULATION

For the experiments to be described below, the following aqueous base was used:

hydroxy methyl propyl cellulose (K100M)	0.5 percent
Kytamer PC (Chitisan)	0.15 percent
U-care JR-400	0.1 percent
Incroquat Behenyl TMS	1.0 percent
Crodamol NM	1.6 percent
Acetulan	2.0 percent
Cremerol HMG	1.0 percent
stearyl alcohol	2.0 percent
allantoin	0.25 percent
Germall Plus	0.3 percent
dimethicone	1.0 percent
(volume/volume)	

and then water was added to bring to volume up to 100 percent. Various antimicrobials were added to this aqueous base, and then tested according to the protocol set forth in Example 1. The results are shown in Table 10.

TABLE 10

Group	*Staphylococcus aureus* (CFU/tube)
aqueous base (control)	5.0×10^8
0.12 % BZK	2.0×10^8
1.0 % PXE	1.0×10^8
0.5 % PXE	3.4×10^8
1.0 % Sensiva	5.0×10^8
0.05% CHG	2.5×10^8
0.3% PHMB	1.0×10^7
1% PXE + 1% Sensiva	1.0×10^8
0.05% CHG + 1% Sensiva	5.0×10^6
0.05% CHG + 1% PXE	1.0×10^8
0.12% BZK + 1% Sensiva	2.5×10^6
0.12% BZK + 1% PXE	1.2×10^7
0.12% BZK + 1% PXE + 1% Sensiva	4.0×10^4
0.12% BZK + 0.5% PXE + 0.05% CHG	2.0×10^5
0.12% BZK + 0.5% PXE + 0.05% CHG + 0.3% PHMB	2.7×10^4
0.12% BZK + 0.5% PXE + 0.05% CHG + 1% Sensiva	0
0.12% BZK + 0.5% PXE + 0.3% PHMB + 1% Sensiva	0
0.12% BZK + 0.5% PXE + 0.05% CHG + 0.3% PHMB + 1% Sensiva	0
negative control (no base/no agent)	8.0×10^8

The foregoing experiments indicate that the potentiation of the antimicrobial activity of agents by Sensiva occurs in aqueous solution, in addition to the results observed using alcoholic gels. A combination of BZK, biguanide (CHG or PHMB), PXE and Sensiva achieved complete kill of test bacteria within 15 seconds.

EXAMPLE 9: SUSTAINED ACTIVITY OF AQUEOUS FORMULATIONS

Various combinations of antimicrobials were incorporated in an aqueous base, as set forth in Example 8, and then tested for sustained activity on leather patches using the protocol set forth in Example 7. The results, which demonstrate enhanced sustained activity in the presence of Sensiva, are shown in Table 11.

TABLE 11

Group	*Staphylococcus aureus* (CFU/patch)
0.12% BZK + 0.5% PXE + 0.05% CHG + 0.3% PHMB	2.0×10^4
0.12% BZK + 0.5% PXE + 0.05%CHG + 0.3% PHMB + 1% Sensiva	0
Aqueous Base (control)	5.0×10^5
Negative Control (no agent/no base)	5.4×10^5

EXAMPLE 10: ALCOHOL GELS CONTAINING SENSIVA AND ZINC ANTI-IRRITANTS

In individuals whose skin is sensitive to alcohol or antiseptics, the use of antimicrobial alcoholic gels can be irritating, and may cause dermatitis. It has been found that certain zinc salts, selected from the group of zinc gluconate, zinc oxide and zinc stearate, can provide an anti-irritant effect (*see* United States Patent No. 5,965,610 by Modak et al., issued October 12, 1999 and United States Patent No. 5,985,918 by Modak et al., issued November 16, 1999). In alcohol gel formulations containing Sensiva, zinc compounds were added in irritation-preventing quantities and their antimicrobial effectiveness was tested. The formulation was as follows:

zinc gluconate	2.0 percent
ethanol (volume/volume)	63.5 percent
Kytamer PC (Chitisan)	0.1 percent
U-care JR 400 (polyquaternium 10)	0.08 percent
Germall Plus	0.3 percent
Crodamol MM	0.9 percent
Acetulan	0.5 percent
Cremerol HMG	1.0 percent
Incroquat	1.5 percent
Polawax A-31	2.0 percent
hydroxy methyl propyl cellulose (K100M)	0.4 percent
zinc stearate	3.5 percent
allantoin	0.2 percent

dimethicone (volume/volume)	0.5 percent
propylene glycol (volume/volume)	1.5 percent
glycerin (volume/volume)	1.0 percent
Sensiva (volume/volume)	1.5 percent
PXE	1.0 percent
BZK	0.12 percent
PHMB	0.3 percent

and water was added to 100% (approx. 18 ml/100 ml formulation). The resulting formulation is referred to as a "cream".

To test for rapid antimicrobial activity, 0.8 ml of the above cream formulation was mixed with 0.1 ml of 10^9/ml CFU of test organisms and 0.1 ml bovine adult serum. After 15 seconds, this mixture was diluted 1000-fold with LTSB drug-inactivating media and 0.5 ml of the resulting solution was subcultured on a TSA plate. The resulting plates were incubated for 24 hours at 37°C and bacterial counts per tube were determined. To test for sustained antimicrobial activity, the method set forth in Example 7, using leather patches, was employed. The results of testing for rapid and sustained antimicrobial activities are shown in Table 12.

TABLE 12

Formulation	Rapid Activity (CFU/tube)	Sustained Activity (CFU/patch
Zn Gluconate 2% + Zn Stearate 3.5% + Sensiva 1.5% + PXE 1% + BZK 0.12% + PHMB 0.3% -containing cream*	0	40
Prevacare	0	9.2×10^3
Cream Without Antimicrobials **	2.8×10^5	8.6×10^3
Control	6.5×10^8	2.3×10^5

* as comprised in the formulation set forth above in this example section.

** the formulation set forth above, omitting Sensiva, PXE, BZK and PHMB

EXAMPLE 11: ANTISEPTIC ALCOHOL GEL FORMULATION CONTAINING ZINC SALTS

The following gel formulation has only a small amount of zinc salts. It was tested for rapid antimicrobial activity against *Staphylococcus* aureus, *Pseudomonas* aeruginosa, and *Escherichia coli* using the protocol set forth in Example 10. The results, which indicate that the formulation has activity against gram positive (*Staphylococcus aureus*) as well as gram negative (*Pseudomonas aeruginosa* and *Escherichia coli*) are shown in Table 13.

ethyl alcohol (volume/volume)	63.5 percent
zinc gluconate	0.8 percent
zinc oxide	0.25 percent
hydroxy methyl propyl cellulose (K100M)	0.4 percent
Glucam P20 (volume/volume)	1.0 percent
Glucam P20 distearate (volume/volume)	1.5 percent
U-care JR400	0.15 percent
silicone (DC 1403) (volume/volume)	1.5 percent
Germall Plus	0.25 percent
PHMB	0.3 percent
PXE	1.5 percent
BZK	0.12 percent
Sensiva	1.5 percent

with water added to 100 percent (approx. 27.2 ml/100 ml).

TABLE 13

Formulation	*S. aureus* CFU/tube	*P. aeruginosa* CFU/tube	*E. coli* CFU/tube
Zn gluconate 0.8% + Zn oxide 0.2 % + PHMB 0.3% + PXE 1.5% + BZK 0.12% + Sensiva 1.5% gel*	0	1.0×10^3	0
Prevacare	0	ND	ND
Alcohol Gel Without Antimicrobials **	3.2×10^5	5.0×10^7	1.0×10^7
Control	8.0×10^8	5.0×10^8	6.5×10^8

* gel formulation set forth above in this example section.

** gel formulation set forth above, lacking PHMB, PXE, BZK and Sensiva.

EXAMPLE 12: FOAMING ANTIMICROBIAL GEL

The following alcoholic foam formulation was prepared and tested for rapid antimicrobial activity according to the method set forth in Example 10, using *Staphylococcus aureus* as the test organism. The results are shown in Table 14. If more foaming is desired, a surfactant, such as lauroyl ethylenediamine triacetic acid sodium salt (0.5-2.0%) may be added to the following formulation.

zinc gluconate	0.25 percent
zinc acetate	0.25 percent
ethanol	65.0 percent
(volume/volume)	
Polyquaternium 22	2.0 percent
Pluronic Gel (F-87)	0.075 percent
(volume/volume)	
BZK	0.12 percent
CHG	0.05%
PXE	1.0 percent
Sensiva	1.0 percent
(volume/volume)	

with water added to 100 percent (approx. 30.25 ml/100 ml).

TABLE 14

Formulation	*S. aureus* CFU/tube
BZK 0.12% + CHG 0.05% + PXE 1.0% + Sensiva 1.0% foam (*supra*)	0
Above Foam Without BZK, CHG, PXE or Sensiva	2.0×10^5
Control	3.9×10^8

EXAMPLE 13: METHOD OF PREPARING HYDROALCOHOLIC GEL COMPOSITIONS

The novel hydroalcoholic gel compositions of the present invention are made according to the following process:

* water phase – one or more hydrogels are dissolved in water at ambient temperature, preferably the hydrogel is present in a concentration of between 0.05 and 0.5 percent and water is present in a concentration of between 15 and 70 percent;

* alcohol phase – one or more emollient are dissolved in alcohol at ambient temperature, preferably the alcohol is present in a concentration between 30 and 95 percent and the emollient is present in a concentration of between 0.2 and 3.0 percent;

* thereafter, the water phase and the alcohol phase are mixed together at ambient temperature;

* once combined, additional compositions can be added, including silicone polymers, thickeners, emulsifiers, emollient solvent and antimicrobial agents.

Hereafter, all percentages should be considered weight/weight percentages, unless specified otherwise.

Each of the following five hydroalcoholic gel compositions were made according to the following method:

- 0.3 % K100M hydrogel was dissolved in water at ambient temperature;
- one or more emulsifiers were dissolved in ethanol at ambient temperature;
- the dissolved hydrogels and dissolved emulsifiers were mixed together at ambient temperature;
- thereafter, the additional ingredients of 2.0 percent glycerin, 0.2 percent silicone glycol (BASF 1066 – DCG Polyol) and antimicrobial agents were added; and
- the total weight of the gel was adjusted to 100 percent without affecting the relative amount of antimicrobial agent.

The amounts of emulsifiers and antimicrobial agents of Samples 1-5 are presented below in Table 15.

TABLE 15

Sample	Emulsifiers	Antimicrobials
1	1% Incroquat + 1% Polawax	1% chlorhexidine
2	2% Incroquat	1% chlorhexidine
3	1% Incroquat	1% chlorhexidine
4	2% Incroquat	0.12% BZK + 0.5% Phenoxyethanol
5	2% Incroquat	None

EXAMPLE 14: ANTIMICROBIAL EFFICACY VARIES USING BASES OF DIFFERENT COMPOSITION

Two commercially available compositions were including in this study: Avagard (Sample 6) and Prevacare (Sample 7). The amounts of thickeners, emulsifiers and antimicrobial agents are set out below in Table 16.

TABLE 16

Sample	Thickeners/Emulsifier	Antimicrobials
6	Beheneth-10 + Behenyl Alcohol + Cetyl Palmitate + Diisopropyl dimer dilinoleate	1% chlorhexidine
7	Stearyl alcohol + coco PG dimonium chloride phosphate + PEG 8000 (carbomer)	0.12% BZK + 0.5% Phenoxyethanol

Samples 1-7 were then evaluated to compare the efficacy of the antimicrobial agents incorporated into different base compositions according to the following method:

- 3 x 3 cm pieces of pigskin were mounted on plastic plate holders of 5 cm diameter with epoxy to expose the skin surface;
- two pieces of skin were used for each sample;
- 0.3 ml of each Sample 1-7 was placed on one of the two pieces;

- the two pieces were rubbed adjacent each other for 30 seconds and dried for 15 minutes at room temperature in an uncovered petridish;
- one of the two pieces was inoculated with 50 µl of a test culture of 10^7 colony-forming units (cfu/ml);
- the inoculated piece was rubbed on the other piece for 15 seconds;
- after 30 seconds, 0.2 ml of LTSB was applied on one of the two pieces;
- the two pieces were rubbed together for 15 seconds and each piece was rinsed with 4.9 ml of LTSB;
- after 1:10 dilution with LTSB, 0.5 ml aliquot was plated on TSA plates;
- plates were inoculated for 24 hours at 37°C; and
- thereafter bacterial cfu per plate were counted.

The results after 15 seconds as part application of the sample are shown below in Table 17.

TABLE 17

Sample	Antimicrobials	Activity (cfu/plate)
5	None	1376
1	1% chlorhexidine	337
2	1% chlorhexidine	320
3	1% chlorhexidine	240
6	1% chlorhexidine	1428
4	BZK + Phenoxyethanol	181
7	BZK + Phenoxycthanol	1760

From these results, it is evident that the antimicrobial effectiveness varies by changing the composition of the base of the present invention. Further, it can be seen that the gel compositions of the present invention (Samples 1-5) provide greater antimicrobial efficacy with equivalent amounts of antimicrobial agents than the in prior art compositions (Samples 6-7). Without being bound to any particular

theory, it is predicted that the thickeners and emulsifiers used in the prior art compositions (Samples 6 and 7) interfere with the antimicrobial agent. It is also notable that Sample 5 of the present invention which did not contain any additional antimicrobial agent yielded better antimicrobial activity than both of the commercially available formulations of Avagard (Sample 6) and Prevacare (Sample 7).

EXAMPLE 15: BROAD SPECTRUM OF ANTIMICROBIAL ACTIVITY

In order to study the spectrum of antimicrobial activity, another hydroalcoholic gel composition (Sample 8) was made according to the following method:

- the hydrogel polyquarternium -10 (U-care JR 30) was dissolved in water at ambient temperature;
- the emulsifiers Incroquot Behenyl TMS and Polawax A31 were dissolved in ethanol at ambient temperature;
- the dissolved hydrogel and dissolved emulsifers were mixed together at ambient temperature;
- thereafter, the emollients Kytamer L and octoxyglycerin; the antimicrobials agents, chlorhexidrine gluconate, benzalkonium chloride, and phenoxyethanol; and silicone glycol (BASF 1066-DCG Polyol) were added.

The amounts of the ingredients specified above for Sample 8 are set forth below in Table 18.

TABLE 18

Ingredients	percentage (w/w)
Water*	30.6
polyquaternium-10 (U-care JR 30)	0.2
Kytamer L	.1
Ethanol	65
Incroquat Behenyl TMS	0.8
Polawax A-31	0.4
octoxyglycerin	2.0
chlorhexidine gluconate	0.05
benzalkonium chloride (BZK)	0.12
phenoxyethanol	0.5
silicone glycol (BASF 1066-DGC Polyol)	0.2

* Water was added to bring the volume up to 100 percent.

Antimicrobial activity was evaluated using the following method comparing Sample 8, Prevacare, Avagard and a control of phosphate-buffered saline:

- sterile pig skin was cut into 3x3 cm sections that were mounted on plastic plate holders of 5 cm diameter with epoxy so that one side was exposed;
- two pieces of skin were used for each sample;
- 30 µl aliquot of the test organism containing 10^7 colony-forming units (cfu/ml) was inoculated on one of the pieces;
- the inoculated piece was rubbed on the other piece for 15 seconds;
- after 5 minutes, 0.3 ml of the test product was applied on one of the two pieces and rubbed onto the other piece for 15 seconds;
- each skin section was rinsed with 4.9 ml of LTSB to recover viable organisms;
- the recovered medium is further diluted 1:10 with LTSB and 0.5 ml aliquot was subcultured on TSA plate;
- the plates were incubated for 24 hours at 37°C?;
- thereafter bacterial cfu per plate were counted.

The results after 15 seconds post-application of each test product are shown below in Table 19.

TABLE 19

Test Organism	CFU per sample treated with			
	Sample 8	Prevacare	Avagard	Control (PBS
S.epidermidis	0	54	70	$9.3x10^4$
S.aureus	0	58	48	$2.3x10^5$
MRSA	0	ND	ND	$9.8x10^3$
VREF	0	ND	ND	$9.4x10^3$
E.aerogenes	0	ND	ND	$9.5x10^3$
A.baumanni	0	ND	ND	$9.3x10^3$
K.pneumoniae	0	ND	ND	$9.3x10^3$
E.coli	0	150	5	$1.9x10^4$
P.aeruginosa	0	0	0	$2.4x10^4$

ND = Not Done

The data shown above indicates that the application of Sample 8 resulted in more effective antibacterial activity than what would have been expected based on the results of the prior art samples of Prevacare and Avagard when tested against *S.epidermidis, S.aureus* and *E.coli.* Also, the data in Table 19 demonstrates an effective antibacterial activity of Sample 8 across a broad spectrum of test organisms.

EXAMPLE 16: SUSTAINED EFFICACY AGAINST *S. AUREUS*

Another hydroalcoholic gel composition made in accordance with this invention (Sample 9) was formulated according to the method set forth in Example 15 above, except that 2.0 percent glycerin was substituted for 2.0 percent octoxyglycerin.

In order to study the sustained efficacy, Samples 8 and 9 were compared with samples of Prevacare, Avagard and a control of 60 percent ethyl alcohol in a gel base with no preservatives, according to the following method:

- sterile pig skin was cut into 3x3 cm sections that were mounted on plastic plate holders of 5 cm diameter with epoxy so that one side was exposed;
- two pieces of skin were used for each sample;
- 0.3 ml aliquot of the test formulation was inoculated on one of the pieces;

- the inoculated piece was rubbed on the other piece for 30 seconds;
- the inoculated piece was left at room temperature for the time period specified below in Table 20;
- after the specified time, 30 µl of *Staphylococcus aureus* containing 10^7 cfu/ml was applied to one of the two pieces and rubbed on the other piece for 15 seconds;
- the samples were subcultured after 30 seconds following the same procedure set forth in Example 15.

The results after 15 minutes, 2 hours, and 3 hours post-application time of Sample 8, Sample 9, Prevacare, Avagard and the control are shown below in Table 20.

TABLE 20

	CFU/sample		
Sample	15 min	2 hours	3 hours
8	31	55	190
9	200	ND	ND
Prevacare	$1.5x10^5$	$9.5x10^3$	$3.1x10^4$
Avagard	$2.6x10^6$	ND	ND
Control	$2.5x10^5$	$9.2x10^3$	$4.0x10^4$

ND = Not Done

The data illustrated in Table 20 above indicates the sustained efficacy of the antimicrobial activity of Samples 8 and 9 which is significantly greater than expected when compared with the samples of Prevacare and Avagard when tested against *S. aureus*.

EXAMPLE 17: RAPID AND SUSTAINED ANTIMICROBIAL EFFICACY DEMONSTRATED *IN VIVO*

In vivo tests were performed on four volunteers to assess the rapid efficacy of hydroalcoholic gel composition (Sample 8) compared with Prevacare, Avagard and a control of phosphate-buffered saline, according to the method

specified below. The order in which the products were tested were varied each of the three times the experiments were repeated. Each volunteer disinfected their hands with 70% ethanol alcohol and dried them thoroughly before beginning the following procedure:

- both hands of each volunteer were inoculated with 1 ml containing 10^6 cfu/ml of *Staphylococcus epidermidis* isolated from each volunteer's flora;
- after 5 minutes, 2 ml of the test product were applied to both hands of each volunteer;
- after 15 seconds the three middle fingers of each hand were rinsed with drug-inactivating media to recover any viable organisms according to the method set forth in Example 15;
- a diluted aliquot of the rinsed solution was plated on a drug-neutralizing (D/E) agar accordingly to the method set forth in Example 15 to count the number of surviving colony forming units.

The results 5 minutes after contaminations with *S. epidermidis* and 15 seconds post-application of the first product are shown in Table 21 below:

TABLE 21

Sample	cfu/ ml (15 sec, post-application of sample)
8	2
Prevacare	66
Avagard	13.3
Control	9600

In vivo tests were performed on the same four volunteers to assess the sustained efficacy of hydroalcoholic gel composition (Sample 8) compared with commercially available formulations of Prevacare, Avagard, Purell (62% ethyl alcohol), Hibiclens (4% chlorhexidine gluconate) and Betadine (10% poviodine iodine with 1% available iodine), and a control (60% ethyl alcohol in a gel base with no preservatives) according to the following method:

- each volunteer disinfected their hands with 70% ethanol alcohol and dried them thoroughly (the order in which the products

were tested was varied each of the three times the experiments were repeated);

- both hands were inoculated with 2 ml containing the test product;
- fifteen minutes after inoculation of the test product, the middle three fingers of one hand were inoculated with 30 µl of *Staphlococcus epidermidis* culture containing 10^7 cfu/ml isolated from each volunteer's own flora;
- after 30 seconds the fingers were rinsed with a drug-inactivating recovery medium according to the method set forth in Example 15;
- a diluted aliquot of the rinsed solution was subcultured on drug-neutralizing agar plates to count the number of surviving colony forming units.

The results 15 minutes after application of the test product and 30 seconds after exposure to *S. epidermidis* are shown below in Table 22:

TABLE 22

Sample	cfu/ ml (30 seconds post exposure)
8	40
Prevacare	$2.1x10^4$
Avagard	$3.1x10^3$
Purell	$2.9x10^4$
Hibiclens	$3.0x10^4$
Betadine	$8.8x10^3$
Control	$1.1x10^4$

The data of Tables 21 and 22 demonstrate the rapid and sustained antimicrobial efficacy of the hydroalcoholic gel composition (Sample 8) made according to the present invention *in vivo* over commercially available products.

EXAMPLE 18: EVEN BETTER RESULTS AT LOWER VISCOSITIES AGAINST *S. AUREUS*

Four additional samples were prepared in accordance with this invention and according to the method of Example 13 having the formulations set forth in Table 23 (Sample 10), Table 24 (Sample 11), Table 25 (Sample 12), and Table 26 (Sample 13) below. The control base was prepared according to formulation set forth in Table 27 (Control). These Samples 10-13 have a lower viscosity than the prior Samples 1-5 and 8-9. The range of viscosity of Samples 1-5 and 8-9 is about 1200 to 1500 cps, with Sample 8 having a viscosity of about 1500 at 20 C. The range of viscosity of Samples 10-13 is 50-200 at 20 C and about 30-50 at 40 C, with Sample 10 being about 55 at 20 C. Viscosity was measured using Brookfield model LVT Spindle No. 2 60 RPM.

Table 23

(Sample 10)

Ingredients	Percentage (w/w)
Water	31.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Incroquat behenyl TMS	0.4
Octoxy Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

Table 24

(Sample 11)

Ingredients	Percentage (w/w)
Water	31.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Incroquat behenyl TMS	0.4
Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12

Phenoxyethanol	0.5

Table 25

(Sample 12)

Ingredients	Percentage (w/w)
Water	33.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Isopropanol	5
Incroquat behenyl TMS	0.4
Octoxy Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

Table 26

(Sample 13)

Ingredients	Percentage (w/w)
Water	26.73
Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Isopropanol	5
Incroquat behenyl TMS	0.4
Glycerin	2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

Table 27

(Control)

Ingredients	Percentage (w/w)
Water	31.73

Polyquaternium-10 (U-careJR30)	0.2
Ethanol	65
Incroquat behenyl TMS	0.4
Octoxy Glycerin	2

The sustained efficacy of these hydroalcoholic gel compositions having lower viscosities (Samples 10, 11, 12, and 13) were compared with Sample 8, Prevacare, Avagard and a control of 60 percent ethyl alcohol in a gel base with no preservatives, according to the following method:

- sterile pig skin was cut into 3x3 cm sections that were mounted on plastic plate holders of 5 cm diameter with epoxy so that one side was exposed;
- two pieces of skin were used for each sample;
- 0.3 ml aliquot of the test formulation was inoculated on one of the pieces;
- the inoculated piece was rubbed on the other piece for 30 seconds;
- the inoculated piece was left at room temperature for 15 minutes;
- after 15 minutes, 30 µl of staphylococcus aureus containing 10^7 cfu/ml was applied to one of the two pieces and rubbed on the other piece for 15 seconds;
- the samples were subcultured after 30 seconds following the same procedure set forth in Example 15.

The results after 15 minutes post-application time of Samples 8, 10, 11, 12 and 13, Purell, Avagard and the control are shown below in Table 20.

TABLE 28

Sample	15 min. (cfu/sample)
8	40
10	0
11	0
12	0

13	0
Purell	1.1×10^5
Avagard	3.9×10^4
Control	2.0×10^5

The data of Table 28 indicates the efficacy of the antimicrobial activity of Samples 8, 10, 11, 12, and 13 in comparison with the prior art products of Purell and Avagard. Further, Samples 10-13, having lower viscosities that Sample 8 demonstrated superior results when tested against *S. aureus*.

EXAMPLE 19: REDUCTION OF HAND FLORA

A surgical scrub was prepared in accordance with this invention and according to the method of Example 13 having the formulation set forth in Table 29 below.

Table 29

(Sample 14)

Ingredients	percentage (w/w)
Water	26.8
U care JR30	0.3
Ethanol	70
Octoxy Glycerin	2
Silicone Glycol (BASF 1066-DCG Polyol)	0.2
Chlorhexidine gluconate	0.05
Benzalkoniumchloride	0.12
Phenoxyethanol	0.5

In order to assess the efficacy of this formation of inhibiting hand flora, Sample 14 was compared with Betadine scrub (10% PVI in non-alcoholic bases) and Avagard, according to the following method:

* each volunteer washed hands with plain soap and water;

* each volunteer applied each of the test products according to the manufacturer's instructions;

** For Betadine --Hands were wet with water; 5 cc of Betadine surgical scrub was poured on the palm of the hand and spread over both the hands; the scrub was rubbed thoroughly over all the areas of the hand for about 5 min; fingernails were thoroughly cleaned; hands were rinsed thoroughly under running water; wash was completed by scrubbing with another 5cc of the Betadine scrub in the same manner;

** For Avagard -- 2 ml of Avagard was dispensed into the palm of one hand; the fingertips of the opposite hand was dipped into the Avagard; the remaining Avagard was spread over the hand just above the wrist; 2ml was dispensed for the other hand and applied in the same manner; another 2ml of Avagard was reapplied on both hands up to the wrist; and

** For Sample 14 -- the method used was same as the method used for Avagard;

* thereafter, each hand was placed in a sterile latex glove;

* one minute after use of the product, 50 ml of sterile phosphate buffered saline (PBS) was added to each glove and the hands were massaged in a uniform manner for one minute;

* the resulting "glove juice" extract was then diluted using a drug inactivating media and subcultured on agar plates to deterine colony counts.

The percent reduction of hand flora one minute after treatment are shown in Table 30 below.

Table 30

Sample	Base Line Counts	1 min. post counts	percent reduction
Sample 14	1.4×10^5	1.3×10^4	90.7
Betadine	2.6×10^5	7.4×10^4	71.6
Avagard	1.4×10^5	1.5×10^5	0

Various publications are cited herein, the contents of which are hereby incorporated herein in their entireties by reference.

WE CLAIM:

1. An antimicrobial composition comprising octoxyglycerin, a quaternary ammonium compound, and an antimicrobial agent selected from the group consisting of a biguanide compound, triclosan, phenoxyethanol, an iodine compound and parachlorometaxylenol.

2. The composition of claim 1 wherein the concentration of octoxyglycerin is between 1 and 5 percent (volume/volume).

3. The composition of claim 1 wherein the concentration of quaternary ammonium compound is between 0.01 and 0.3 percent.

4. The composition of claim 2 wherein the concentration of quaternary ammonium compound is between 0.01 and 0.3 percent.

5. The composition of claim 1 or 2 wherein the antimicrobial agent is a biguanide compound at a concentration of between 0.05 and 4 percent.

6. The composition of claim 5 wherein the biguanide compound is a chlorhexidine compound.

7. The composition of claim 3 or 4 wherein the antimicrobial agent is a biguanide compound at a concentration of between 0.05 and 4 percent.

8. The composition of claim 7 wherein the biguanide compound is a chlorhexidine compound.

9. The composition of claim 1 wherein the antimicrobial agent is triclosan at a concentration of between 0.1 and 2 percent.

10. The composition of claim 2 wherein the antimicrobial agent is triclosan at a concentration of between 0.1 and 2 percent.

11. The composition of claim 3 wherein the antimicrobial agent is triclosan at a concentration of between 0.1 and 2 percent.

12. The composition of claim 4 wherein the antimicrobial agent is triclosan at a concentration of between 0.3 and 2 percent.

13. The composition of claim 1 wherein the antimicrobial agent is phenoxyethanol at a concentration of between 0.3 and 2 percent.

14. The composition of claim 2 wherein the antimicrobial agent is phenoxyethanol at a concentration of between 0.3 and 2 percent.

15. The composition of claim 3 wherein the antimicrobial agent is phenoxyethanol at a concentration of between 0.3 and 2 percent.

16. The composition of claim 4 wherein the antimicrobial agent is phenoxyethanol at a concentration of between 0.3 and 2 percent.

17. The composition of claim 1 wherein the antimicrobial agent is parachlorometaxylenol at a concentration of between 0.3 and 2 percent.

18. The composition of claim 2 wherein the antimicrobial agent is parachlorometaxylenol at a concentration of between 0.3 and 2 percent.

19. The composition of claim 3 wherein the antimicrobial agent is parachlorometaxylenol at a concentration of between 0.3 and 2 percent.

20. The composition of claim 4 wherein the antimicrobial agent is parachlorometaxylenol at a concentration of between 0.3 and 2 percent.

21. The antimicrobial composition of claim 1 which further comprises between 20 and 85 percent (volume/volume) of ethanol.

22. The antimicrobial composition of claim 1 which further comprises between 20 and 85 percent (volume/volume) of isopropanol.

23. The antimicrobial composition of claim 1, 2 or 3 which further comprises between 3 and 10 percent (volume/volume) hexanol.

24. The antimicrobial composition of claim 1 which further comprises between 0.2 and 7 percent of a zinc compound selected from the group consisting of zinc gluconate, zinc oxide, zinc acetate, zinc stearate and zinc salicylate.

25. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 0.2 percent of benzalkonium chloride, and between 0.5 and 4 percent of chlorhexidine digluconate.

26. The antimicrobial composition of claim 25 which further comprises between 20 and 85 percent (volume/volume) of ethanol.

27. The antimicrobial composition of claim 25 which further comprises between 20 and 85 percent (volume/volume) of isopropanol.

28. The antimicrobial composition of claim 25 which further comprises between 3 and 10 percent (volume/volume) hexanol.

29. The antimicrobial composition of claim 25 which further comprises between 0.2 and 7 percent of a zinc compound selected from the group consisting of zinc gluconate, zinc oxide, zinc stearate and zinc salicylate.

30. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of a chlorhexidine compound, and between 1 and 2 percent of miconazole.

31. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of a chlorhexidine compound, and between 0.3 and 1 percent polymixin.

32. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of a chlorhexidine compound, and between 0.1 and 0.5 percent neomycin.

33. The composition of claim 32, further comprising between 0.3 and 1 percent polymixin.

34. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of a chlorhexidine compound, and between 1 and 2 percent silver sulfadiazine.

35. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of chlorhexidine digluconate, and between 1 and 2 percent of miconazole.

36. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of chlorhexidine digluconate, and between 0.3 and 1 percent polymixin.

37. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of chlorhexidine digluconate, and between 0.1 and 0.5 percent neomycin.

38. The composition of claim 37, further comprising between 0.3 and 1 percent polymixin.

39. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 4 percent of chlorhexidine digluconate, and between 1 and 2 percent silver sulfadiazine.

40. An antimicrobial composition comprising between 1 and 5 percent (volume/volume) octoxyglycerin, between 0.05 and 2 percent of chlorhexidine digluconate, between 0.3 and 2 percent of phenoxyethanol, between 0.01 and 0.3 percent of a quaternary ammonium compound, and between 20 and 85 percent of an alcohol selected from the group consisting of ethanol and isopropyl alcohol.

41. A hydroalcoholic gel composition comprising between 30 and 95 percent (weight/weight) alcohol, 15 and 70 percent (weight/weight) water, 0.05 and 0.5 percent (weight/weight) hydrogel, and 0.2 and 3.0 percent (weight/weight) emollient, wherein said composition has a viscosity below 2000 centipoises.

42. The composition of claim 41 which further comprises between 0.05 and 0.5 percent emulsifier.

43. The composition of claim 41 which further comprises between 0.1 and 1.0 percent silicone polymer.

44. The composition of claim 41 which further comprises between 0.5 and 5.0 percent emollient solvent.

45. The composition of claim 41 which further comprises between 0.1 and 1.0 percent thickening agent.

46. The composition of claim 41 further comprising an antimicrobial agent.

47. The composition of claim 41 wherein the hydrogel is selected from the group consisting of one or more than one of hydroxypropylmethyl cellulose, cationic hydroxyethyl cellulose, ethyl cellulose, hydroxypropyl cellulose, hydroxymethyl cellulose, carboxymethyl cellulose, polymethylene oxide, and chitosan pyrrolidone carboxylate.

48. The composition of claim 41 wherein the emollient is selected from the group consisting of one or more than one of PEG 20 Almond Glycerides, Probutyl DB-10, Glucam P20, Glucam E-10, Glucam P-10, Glucam E-20, Glucam P-20 distearate, Glycerin, Propylene glycol, oxtoxy glycerin, cetyl acetate and acetylated lanolin alcohol, cetyl ether, myristyil ether, hydroxylated milk glycerides, polyquaternium compounds, chitosan, copolymer of dimethyl dialyl ammonium chloride and acrylic acid, dipropylene glycol methyl ethers, and polypropylene glycol ethers.

49. The composition of claim 42 wherein the emulsifier is selected from the group consisting of one or more than one of Incroquat Behenyl TMS-50, Polawax, Stearyl alcohol, and cetearyl alcohol.

50. The composition of claim 43 wherein the silicone polymer is selected from the group consisting of one or more than one of polydimethylsiloxane polymer, dimethiconol fluid in dimethicone, cyclomethicone and dimethicone copolyl, and silicone glycol.

51. The composition of claim 44 wherein the emollient solvent is selected from the group consisting of one or more than one of glycidyl ethers having alkyl chains up to and including 18 carbon molecules and ethoxylates and propoxyltes thereof, glyceryl ethers having alkyl chains up to and including 18 carbon molecules and ethoxylates and propoxylates thereof, mono- and diglyceryl ethers having alkyl chains up to and including 18 carbon molecules and ethoxylates and propoxylates thereof, ethoxylate and propoxylate ethers, ethoxy diglycol esters, ethyl hexyl alcohol propoxylate, and propylene glycol esther ethoxylates and propoxylates.

52. The composition of claim 45 wherein the thickening agent is selected from the group consisting of one or more than one of crothix, crodamol and behenyl alcohol.

53. The composition of claim 46 wherein the antimicrobial agent is selected from the group consisting of one or more than one of biguanides, phenols, quaternary ammonium compounds and anti-fungal agents.

54. The composition of claim 53 wherein chlorhexidine gluconate is the biguanide.

55. The composition of claim 53 wherein triclosan is the phenol.

56. The composition of claim 53 wherein benzalkonium chloride is the quaternary ammonium compound.

57. The composition of claim 53 wherein povidone iodine is the anti-fungal agent.

58. The composition of claim 46 wherein phenoxyethanol is the antimicrobial agent.

59. The composition of claim 41 wherein the alcohol is selected from the group consisting of one or more than one of aliphatic alcohol, fatty alcohol and hexanol.

60. The composition of claim 59 wherein the aliphatic alcohol is selected from the group consisting of one or more than one of ethanol, isopropyl alcohol or n-propyl alcohol.

61. The composition of claim 59 wherein the fatty alcohol is elected from the group consisting of one or more than one cetyl, myrstyl, stearyl, octyl, decyl, and lauryl alcohol.

62. The composition of claim 59 wherein the aliphatic alcohol is ethanol at a concentration of between 60 and 95 percent.

63. The composition of claim 59 wherein the fatty alcohol is present at a concentration of between 0.5 and 5%.

64. The composition of claim 59 wherein the hexanol is present at a concentration of between 3 and 5 percent.

65. The composition of claim 59 wherein the aliphatic alcohol is isopropanol at a concentration of between 60 and 95 percent.

66. The composition of claim 49 wherein Incroquat Behenyl TMS and Polawax are present in a 1:1 ratio.

67. The composition of claim 47 wherein the hydroxypropyl methyl cellulose and cationic hydroxy ethyl cellulose are present in a 1:1 ratio.

68. The composition of claim 47 wherein hydroxypropyl methyl cellulose and chitosen pyrrolidone carboxylate and present in a 1:1 ratio.

69. The composition of claim 48 wherein propylene glycol and glycerin are present in a 1:1 ratio.

70. The composition of claim 48 wherein propylene glycol and octoxyglycerin are present in a 1:1 ratio.

71. The composition of claim 53 wherein the biguanide is chlorhexidine gluconate at a concentration of between 0.05 and 0.5 percent, wherein the quaternary ammonium compound is benzalkanium chloride at a concentration of between 0.1 and 0.25 percent, and wherein the phenol is phenoxyethanol at a concentration of between 0.1 and 1.0 percent.

72. The antimicrobial composition of claim 27 which further comprises between 5 and 20 percent (volume/volume) of n-propyl alcohol.

73. The composition of claim 65 which further comprises between 5 and 20 percent (weight/weight) of n-propyl alcohol.

74. A method of preparing a hydroalcoholic gel composition comprising the steps of:

- dissolving a hydrogel in water at ambient temperature,
- dissolving an emulsifier in an alcohol at ambient temperature, and
- mixing said dissolved hydrogel and said dissolved emulsifier at an

ambient temperature,

wherein said composition has a viscosity below 2000 centipoises at between 20 and 40 °C.

73. The method of claim 73 further comprising a subsequent step of:

- adding to the mixture one or more emollients, one or more silicone

polymers, one or more emollient solvents, one or more antimicrobial agents, or one or more thickening agents, or mixtures thereof.

NOTIFICATION OF DECISION CONCERNING REQUEST FOR RECTIFICATION

International application No.
PCT/US02/33865

This communication is in reply to applicant's paper filed in the Patent and Trademark Office on
24 OCT 2002

Applicants' 24 OCT 2002 "Request For Rectification" forwarding sheets nos. 28 and 29 of the description has been received.

The proposed replacement sheets of the description include changes made therein apart from what is permitted for the rectification of obvious errors under PCT Rule 91.1. Specifically:

Sheets nos. 28 and 29: material added to tables 2 and 3.

Obvious errors may be corrected pursuant to PCT Rule 91.1. However, the "rectification itself shall be obvious in the sense that anyone would immediately realize that nothing else could have been intended than what is offered as the rectification". Rule 91.1(b). In the present case, the changes proposed above are not rectifications permitted under Rule 91.1(b), as anyone would not immediately realize that nothing else could have been intended than what is offered as the rectification. The changes described above are not immediately obvious to anyone. Therefore, a careful evaluation of each of the changes made to the original disclosure by one skilled in the art is required.

Accordingly, proposed replacement sheets nos. 28 and 29 of the description are REFUSED.

Note that during Chapter I proceedings, changes to the description, claims and drawings may only be entered upon approval by the International Searching Authority if the changes comply with Rule 91.1(b). However, applicant may submit these changes for consideration as an amendment under PCT Article 34 along with the Demand when entering Chapter II under the provisions of the Patent Cooperation Treaty, or by submitting the changes upon entry in the National Stage. The amendments may only be entered if they do not go beyond the disclosure of the international application as filed. Additionally, Article 34 amendments submitted during Chapter II must also be in compliance with PCT Rules 11.14 and 66.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/33865

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 7/32,7/34, 7/36, 7/38, 31/79, 7/00

US CL : 424/65, 66, 67, 68, 78.02, 78.08, 400, 401

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/65, 66, 67, 68, 78.02, 78.08, 400, 401

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN

search terms: octoxyglycerin, antibiotic, miconzolin, neomycin

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,E	US 6,397,357 A (CHOPRA et al.) 14 May 2002, see entire document.	1-73
Y,E	US 6,426,062A (CHOPRA et al.) 30 July 2002 see entire document.	1-73

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
18 NOVEMBER 2002	22 MAY 2003
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Form PCT/ISA/210 (second sheet) (July 1998)*